UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

LEON D. BOROCHOFF, on behalf of himself and all other similarly situated,	:	
Plaintiff,	:	CIVIL ACTION
v.	:	NO. 07-CIV-5574 (LLS)
GLAXOSMITHKLINE PLC, et al.,	:	
Defendants.	:	

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' MOTION TO DISMISS AMENDED COMPLAINT

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In their Amended Complaint ("Complaint"), Lead Plaintiff Avon Pension Fund, Administered by Bath & North East Somerset Council ("Avon Pension Fund"), and plaintiffs Plumbers & Steamfitters Local 773 Pension Fund ("Plumbers & Steamfitters Local 773") and Plumbers' Union Local No. 12 Pension Fund ("Plumbers' Union Local No. 12") (collectively "plaintiffs")[1] seek damages for alleged violations of Section 10(b) of the Securities Exchange Act of 1934 ("Exchange Act"), Rule 10b-5 promulgated thereunder by the Securities and Exchange Commission ("SEC"), and Section 20(a) of the Exchange Act. Plaintiffs purport to represent a class of all purchasers of GlaxoSmithKline plc's ordinary shares, traded on the London Stock Exchange, and American Depository Shares ("ADSs"), traded on the New York Stock Exchange, between October 27, 2005 and May 21, 2007 (the putative "Class Period").

Pursuant to the Private Securities Litigation Reform Act of 1995 ("PSLRA"), 15 U.S.C. § 78u-4(b), and Federal Rules of Civil Procedure 12(b)(6) and 9(b), defendants GlaxoSmithKline plc ("GSK" or "the Company"),[2] Jean-Pierre Garnier, Ph.D., David Stout,

[1] By Order dated October 5, 2007, the Court appointed Avon Pension Fund as Lead Plaintiff and appointed attorneys from the law firm of Coughlin Stoia Geller Rudman & Robbins LLP as Lead Counsel. When Lead Counsel filed the Amended Complaint on November 13, 2007, they added Plumbers & Steamfitters Local 773 and Plumbers' Union Local No. 12 as named plaintiffs. Courts have construed the PSLRA as permitting Lead Counsel to add named plaintiffs at this stage of the litigation. *See, e.g., In re Worldcom, Inc. Sec. Litig.*, 219 F.R.D. 267, 286 (S.D.N.Y. 2003). Defendants reserve their rights, however, to challenge all three plaintiffs' adequacy to serve as class representative and to oppose certification of a class in this action should the Court deny defendants' motion to dismiss.

[2] GlaxoSmithKline plc is a public limited company incorporated under the laws of England and Wales. The Company was created in December 2000 by the merger between Glaxo Wellcome plc and SmithKline Beecham plc. (See Compl. ¶¶ 9, 20; Exh. 2, GSK 2005 Form 20-F (filed 03/03/06), at 4.) The bulk of the actions the Complaint ascribes to "GSK" (assuming they occurred at all) are actually attributable to SmithKline Beecham Corporation d/b/a GlaxoSmithKline, of which GlaxoSmithKline plc is the indirect, ultimate parent, and not to GlaxoSmithKline plc itself. SmithKline Beecham Corporation d/b/a GlaxoSmithKline is a corporation organized under the laws of the Commonwealth of Pennsylvania, with a principal place of business in Philadelphia, Pennsylvania. To avoid unnecessary confusion, and for purposes of this brief only, defendants will use "GSK" to encompass both GlaxoSmithKline plc and SmithKline Beecham Corporation d/b/a GlaxoSmithKline (or, to the extent appropriate, any of the other entities of which GlaxoSmithKline plc is the indirect, ultimate parent).

Julian Heslop and Simon Bicknell ("Individual Defendants")[3] (collectively "defendants"), by their attorneys, respectfully submit this memorandum of law in support of their motion to dismiss plaintiffs' Complaint.

I. INTRODUCTION[4]

GSK creates, discovers, develops, manufactures and markets prescription medications, as well as other pharmaceutical products and healthcare products. In 1999, the United States Food and Drug Administration ("the FDA" or "the Agency") approved GSK's prescription medication Avandia® (rosiglitazone) for the treatment of type 2 diabetes. Since then, the Company and the FDA have continued to monitor the safety of Avandia, and, on several occasions prior to the events giving rise to this lawsuit, they have worked together to update Avandia's product labeling to reflect new safety data.

Through clinical trials, and in the course of its continued post-approval pharmacovigilance[5] efforts, GSK sought to investigate Avandia's safety profile, including

[3] The Complaint alleges that the Individual Defendants held the following positions at GSK during the time period in question: Dr. Jean-Pierre Garnier, Chief Executive Officer; David Stout, President, Pharmaceutical Operations; Julian Heslop, Chief Financial Officer; and Simon Bicknell, Company Secretary. (*See* Compl. ¶¶ 10-13.)

[4] The Statement of Facts, Section II below, describes the events outlined in this Introduction in more detail, providing citations to the Complaint and documents the Court may consider on a motion to dismiss. *See infra* n.13 and Section III.C. Definitions of certain medical and pharmaceutical research terms that are used throughout this memorandum are set forth in footnotes to this Introduction.

[5] According to FDA industry guidance, "[p]harmacovigilance principally involves the identification and evaluation of safety signals." (Exh. 13, U.S. Dep't of Health & Human Servs., FDA, CDER, CBER Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment at 4 (March 2005, http://www.fda.gov/cder/guidance/6359OCC.pdf (hereinafter "FDA Pharmacovigilance Guidance").) The term "safety signal" in this context "refers to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use." (*Id*.) Such signals "generally indicate the need for further investigation, which may or may not lead to the conclusion that the product caused the event. After a signal is identified, it should be further assessed to determine whether it represents a potential safety risk and whether other action should be taken." (*Id*.)

whether there was an association between the use of Avandia and ischemic cardiac events.[6] Beginning in 2005, the Company conducted pooled statistical analyses – commonly referred to as a "meta-analysis"[7] – of data from previously conducted randomized, controlled clinical trials[8] that had not been designed to examine Avandia's cardiovascular risk. GSK also commissioned an observational cohort study[9] of 33,363 patients using a medical and pharmacy claims database ("Balanced Cohort Study"). While the results of the meta-analysis of these clinical trials observed an increased risk for myocardial ischemia, the Balanced Cohort Study showed no such increased risk.

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[6] The term "ischemia" means "[r]educed blood flow to an organ, usually due to a constricted or blocked artery." (Exh. 43, The American Heart Association's Cardiac Glossary, http://americanheart.org/presenter.jhtml?identifier=3038598 (hereinafter "Cardiac Glossary").) An "ischemic stroke" refers to "[t]he death of or injury to brain cells caused when a blood clot or other particle blocks an artery in the brain (cerebral artery) or leading to it, such as the carotid (neck) artery." (*Id.*) "Myocardial ischemia" is "[a] condition in which there is not enough blood flow (and thus oxygen and nutrient supply) to the heart muscle." (*Id.*) And "myocardial infarction" – the medical term for heart attack – "is the damaging or death of an area of the heart muscle (myocardium) resulting from a blocked blood supply to that area." (*Id.*) These ischemic cardiac events should not be confused with "congestive heart failure," a non-ischemic condition which occurs when the heart is unable to pump enough blood to meet the needs of the body's other organs. (*Id.*)

[7] The FDA defines "meta-analysis" as "the process or technique of synthesizing research results by using various statistical methods to retrieve, select, and combine results from previous separate but related studies which on their own are not large enough to examine a particular question." (Exh. 15, Statement of FDA Comm'r, Andrew C. von Eschenbach, M.D., before the United States House of Representatives' Committee on Oversight and Government Reform at 15 (dated 06/06/07), http://oversight.house.gov/documents/20070606105302.pdf (hereinafter "von Eschenbach Statement"), *paraphrased in* Compl. ¶ 25 n.3.) As the FDA has explained, although meta-analyses "are often informative," they also have "important limitations." (*Id.*) For example, meta-analyses are "complicated to conduct," and "[d]eciding the best methods of combining data, which studies to combine, and similar decisions can be controversial." (*Id.* at 15-16.) Accordingly, while the FDA will consider safety information derived from meta-analyses, it "has historically been cautious in the use of meta-analyses in support of regulatory decisions." (*Id.* at 16.)

[8] A "clinical trial" is "a research study to answer specific questions about vaccines or new therapies or new ways of using known treatments." (Exh. 44, ClinicalTrials.gov, Glossary of Clinical Trials Terms ("hereinafter "Clinical Trials Glossary"), http://clinicaltrials.gov/ct/info/glossary Clinical trials.) "Clinical trials are used to determine whether new drugs are safe and effective." (*Id.*) A "controlled" clinical trial means that "one group of participants is given an experimental [medication], while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo." (*Id.*) A "randomized trial" is "a study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms [groups] of a clinical trial." (*Id.*)

[9] Through such observational, or pharmacoepidemiologic, studies, a pharmaceutical manufacturer can evaluate a safety signal in the "real world" use of the medicine. (*See* Exh. 13, FDA Pharmacovigilance Guidance at 12-15 (discussing pharmacoepidemiologic studies).)

Beginning in October 2005, GSK shared its meta-analysis results with the FDA as they became available. By August 2006, GSK had submitted the Final Reports for the meta-analysis and the Balanced Cohort study to the FDA, and, in or about October 2006, posted the results on GSK's publicly available Clinical Trial Register ("CTR"). Also in late 2006, the results of two large, long-term clinical trials, known as the DREAM and ADOPT studies, were published in peer-reviewed journals. The DREAM study showed no statistically significant difference between the Avandia group and the placebo group with respect to cardiovascular events. Similarly, the ADOPT study did not show an increased risk of ischemic events in the use of Avandia relative to other anti-diabetic medications studied in the trial (metformin and glyburide).[10]

Because meta-analysis as a methodology has well recognized limitations and is used with caution by the FDA, and because GSK's meta-analysis results conflicted with the results of other, more reliable studies, the FDA undertook a full assessment of the data and initiated its own meta-analysis to confirm GSK's results. In April 2007, the Agency began to work on a communication strategy for advising the public of a potential cardiovascular safety issue with respect to Avandia. On May 16, 2007, the FDA met with GSK to further analyze the data. The Agency also planned to schedule an Advisory Committee meeting in the late summer or early fall of 2007 to seek expert advice as to how to interpret the inconsistent data.[11]

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[10] Subsequently, in June 2007, interim results from another large, long-term clinical trial, RECORD, were published. These interim results did not show an increased cardiovascular risk with Avandia when compared to two other anti-diabetic medications.

[11] The FDA uses advisory committees "to obtain outside advice and opinions from expert advisors so that final agency decisions will have the benefit of wider national expert input." (Exh. 12, U.S. Dep't of Health & Human Servs., FDA, CDER, The CDER Handbook 11 (last revised 03/16/98), http://www.fda.gov/cder/handbook (hereinafter "CDER Handbook").) The Agency may seek an advisory committee's advice about, *inter alia*, "a new drug, a major indication for an already approved drug, or a special regulatory requirement being considered, such as

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Before the FDA could complete its evaluation of the available Avandia data, however, *The New England Journal of Medicine*, on May 21, 2007, published on its website the results of a separate meta-analysis, conducted by Steven E. Nissen, M.D., and Kathy Wolski, M.P.H., which, like GSK's meta-analysis, observed an increased cardiac ischemic risk with Avandia.[12] Nissen obtained data for his meta-analysis from GSK's publicly available CTR.

With the publication of the Nissen article, the FDA accelerated its public message by issuing a "safety alert" the same day, advising that the Agency was aware of a "potential" safety issue related to Avandia. (Exh. 26, FDA Press Release, FDA Issues Safety Alert on Avandia (May 21, 2007) (hereinafter "FDA Safety Alert") (emphasis added), *cited in* Compl. ¶¶ 31, 65 (omitting most of text).) The Safety Alert went on to stress that the "FDA ha[d] ***not*** confirmed the clinical significance of the reported increased risk in the context of other studies" and that it was "***not*** asking [GSK] to take any specific action at this time." (*Id*. (emphasis added).)

Plaintiffs nevertheless seized on the fact of the Nissen article and the FDA Safety Alert (and a subsequent decline in GSK's stock price), and, on June 11, 2007, filed this action, alleging that defendants had committed securities fraud by not disclosing GSK's meta-analysis before the FDA issued its Safety Alert. More specifically, plaintiffs contend that certain "positive" public statements made by GSK between October 27, 2005 and May 21, 2007 (the

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a boxed warning in a drug's labeling." (*Id*.) While advisory committee recommendations are not binding on the FDA, "the agency considers them carefully when deciding drug issues." (*Id*.)

[12] *See* Exh. 37, Steven E. Nissen, M.D., and Kathy Wolski, M.P.H., *Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes*, 356 N. Engl. J. Med. 2457, 2457-59 (June 14, 2007) (published online May 21, 2007), http://content.nejm.org/cgi/reprint/356/24/2457.pdf (hereinafter "Nissen Article".) The *New England Journal of Medicine* published the print version of the Nissen article on June 14, 2007.

putative "Class Period") were materially false and misleading because they did not also mention the preliminary meta-analysis results (submitted to the FDA in October 2005) or the final meta-analysis results (submitted to the FDA in August 2006).

The Complaint does nothing, however, to support such a theory of liability with the fact pleading required by Rule 9(b) and the Private Securities Litigation Reform Act of 1995 ("PSLRA").

First, plaintiffs have in no way established that defendants had any duty to disclose GSK's meta-analysis to the investing public. A pharmaceutical company has no obligation to disclose safety information about a medication where the information is inconclusive and the company does not have a significant reason to believe that the product's commercial viability is at risk. *E.g., In re Carter-Wallace, Inc. Sec. Litig.*, 150 F.3d 153, 157 (2d Cir. 1998) (*Carter-Wallace I*); *In re Bayer AG Sec. Litig.*, No. 03-Civ-1546, 2004 WL 219357 (S.D.N.Y. Sept. 30, 2004). Here, the very document upon which plaintiffs rely – the FDA Safety Alert – plainly states that the available data regarding Avandia's cardiovascular risk were "contradictory," not conclusive, and that the FDA itself had ***not*** determined the clinical significance of GSK's meta-analysis.

Second, the Complaint's "scienter" allegations come nowhere close to satisfying the requirements of the PSLRA. The Complaint pleads ***no*** facts to suggest fraudulent intent, never mind "facts that give rise to a 'strong' – e.g., a powerful or cogent – inference" that defendants acted with fraudulent intent. *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 127 S. Ct. 2499, 2510 (2007). The Complaint instead rests almost entirely on the sort of conclusory allegations that courts routinely find legally deficient. Further, plaintiffs' theory that defendants were trying to deceive anyone is implausible on its face. Indeed, the very information plaintiffs

claim defendants fraudulently concealed, was, in fact, disclosed to the FDA and other regulatory agencies, and posted on the Company's CTR.

Third, many of the statements plaintiffs have identified as "false and misleading" are forward looking statements about the future prospects of Avandia. Thus, without any factual allegations showing that defendants had "actual knowledge" that those statements were false, the statements fall within the PSLRA's "safe harbor" and are not actionable as a matter of law.

For each of these separate and independent reasons, discussed more fully below, plaintiffs' claims should be dismissed.

II. STATEMENT OF FACTS[13]

To fully and fairly assess the sufficiency of plaintiffs' allegations, particularly under the Supreme Court's recent decision in *Tellabs*, 127 S. Ct. at 2509, the Court should take into account the regulatory context in which Avandia's cardiovascular safety profile has been evaluated and monitored, as presented in publicly available documents of which the Court may take judicial notice. (*See infra* note 35 and Section III.C.)[14] This regulatory environment is part

[13] This Statement of Facts is drawn from the Complaint's factual allegations, which are accepted as true solely for purposes of this motion, and only to the extent the allegations do not contradict documents considered to be part of the complaint or amenable to judicial notice. *In re Yukos Oil Co. Sec. Litig.*, No. 04-CV-5243, 2006 WL 3026024, at *12 (S.D.N.Y. Oct. 25, 2006) ("The Court need not accept as true any allegations that are contradicted by documents deemed to be part of the complaint, or materials amenable to judicial notice."); *accord In re Aegon N.V. Sec. Litig*., No. 03-CV-0603, 2004 WL 1415973, at *5 (S.D.N.Y. June 23, 2004); *Rapoport v. Asia Elecs. Holding Co., Inc.*, 88 F. Supp. 2d 179, 184 (S.D.N.Y. 2000); *In re Hunter Envtl. Servs. Inc. Sec. Litig.*, 921 F. Supp. 914, 918-19 (D. Conn. 1996). As explained in Section III.C, below, the Court may consider the full text of any documents quoted or referenced in the Complaint, materials upon which plaintiffs relied in bringing this suit, and matters of which judicial notice may be taken under Federal Rule of Evidence 201, including, *inter alia*, public documents filed with the SEC and public statements issued or made on behalf of governmental agencies such as the FDA. Accordingly, defendants are submitting in support of their motion an appendix of exhibits they believe the Court may properly consider when deciding this motion. *See* Appendix accompanying the Affidavit of Gay Parks Rainville in Support of Defendants' Motion to Dismiss Amended Complaint.

[14] *See, e.g., In re Discovery Labs. Sec. Litig.*, No. 06-1820, 2006 WL 3227767 (E.D. Pa. Nov. 1, 2006) (evaluating sufficiency of Rule 10b-5 allegations within regulatory context); *In re Discovery Labs. Sec. Litig.*, No. 06-1820, 2007 WL 789432 (E.D. Pa. Mar. 15, 2007) (same); *Noble Asset Mgmt. v. Allos Therapeutics, Inc.*, No.

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of the total mix of information available to the securities markets, and provides the context in which specific information is evaluated. In attempting to assert their claims, plaintiffs have ignored or misstated this regulatory environment. Therefore, defendants provide below a brief overview of this regulatory context and a summary of the relevant Avandia regulatory events.

A. Overview Of Relevant FDA Regulatory Process

1. Post-Approval Safety Monitoring

After approving a medication, the FDA continues to monitor its safety, primarily through the Division of Pharmacovigilance and Epidemiology of the FDA's Center for Drug Evaluation and Research. (Exh. 12, CDER Handbook at 42-48.) The Agency accomplishes this monitoring function "by reassessing drug risks based on new data learned after the drug is marketed, and recommending ways of trying to most appropriately manage that risk." (*Id.* at 42.) Accordingly:

> As new information related to a marketed drug becomes available, the Agency reviews the data and evaluates whether there is a potential drug safety concern. When a potential drug safety concern arises, relevant scientific experts within the Agency engage in a prompt review and analysis of available data. Often, there is a period of uncertainty while FDA evaluates the new safety information to determine whether there is an important drug safety issue related to a specific drug or drug class and whether regulatory action is appropriate. During this period, FDA also is actively engaged in scientific efforts to gather additional safety information. The Drug Safety Oversight Board may be consulted and provide recommendations to the Director of the Center for Drug Evaluation and Research regarding the management and communication of an emerging drug safety issue. FDA also may consult an Advisory Committee regarding an emerging drug safety issue. Sponsors are also evaluating the new safety information and

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CIVA-04-CV-1030, 2005 WL 4161977 (D. Colo. Oct. 20, 2005) (same); *In re Medimmune, Inc. Sec. Litig.*, 873 F. Supp. 953 (D. Md. 1995) (same).

> providing the results of their analyses to FDA during this time. As additional data relevant to an emerging drug safety issue become available (e.g., data from an ongoing study or data from available clinical databases), such data are considered in the analysis and decision-making process. Upon evaluation of additional data, further regulatory action, such as a revision to product labeling or a Risk Minimization Action Plan (RiskMAP), may be appropriate.

(Exh. 14, U.S. Dep't of Health & Human Serv., FDA, CDER Guidance: Drug Safety Information – FDA's Communication to the Public at 4 (March 2007), http://www.fda.gov/cder/guidance/7477fnl.pdf (hereinafter "FDA Public Communication Guidance").)

2. Communication Of Emerging Safety Information

The FDA uses the term "emerging drug safety information" to describe information the Agency "is monitoring or analyzing that may have the potential to alter the benefit/risk analysis for a drug in such a way as to affect decisions about prescribing or taking the drug (i.e., an important drug safety issue), but that has not yet been fully analyzed or confirmed." (Exh. 14, FDA Public Communication Guidance at 5.) The Agency may derive such information "from data from postmarketing surveillance (for example, reported serious adverse drug experiences[15]), clinical studies, clinical pharmacology studies, epidemiological studies, or the scientific literature." (*Id*.) While the FDA will consider safety information derived from meta-analyses, it "has historically been cautious in the use of meta-analyses in support of regulatory decisions." (Exh. 15, von Eschenbach Statement at 15-16.) Meta-analyses have "important limitations." (*Id*.) They are "complicated to conduct," and "[d]eciding the best

[15] "Serious adverse drug experiences" include, *inter alia*, "[a]ny adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect." 21 C.F.R. § 314.80(a).

methods of combining data, which studies to combine, and similar decisions can be controversial." (*Id*. at 16.)

Only ***after*** the FDA completes its own evaluation of available post-marketing safety data, will it disseminate emerging safety information to the public. (*See* Exh. 14, FDA Public Communication Guidance at 5.) In some cases, however, the FDA will make the information publicly available after it has analyzed the data but "before having reached a decision about the need for a regulatory action." (*Id*.)

In evaluating an emerging safety concern and deciding whether to make such information available to the public, the Agency considers many factors, including the following:

- Reliability of the data
- Magnitude of the risk
- Seriousness of the event (e.g., severity and reversibility) relative to the disease being treated
- Plausibility of a causal relationship between the use of a drug and the adverse event
- Extent of patient exposure (e.g., how broadly is the drug used)
- Potential to prevent or mitigate the risk in the patient population (e.g., monitoring)
- Effect on clinical practice
- Disproportionate impact on particular populations (e.g., children or the elderly)

(*Id*.) Making this information available, however, "does not necessarily mean that FDA has concluded there is a causal relationship between the drug and the adverse events described" or "that FDA is advising healthcare professionals to limit their prescribing of the drug at issue." (*Id*. at 6.)

Although the FDA is "committed to early communication of emerging information about the safety of medical products," it recognizes that "any communication must be responsible and measured, taking into account the impact that the message will have on patients and practitioners alike, to encourage good health care choices, and help avoid bad ones." (Exh. 15, von Eschenbach Statement at 4.)

B. Relevant Avandia Regulatory Events

1. FDA Approval

In May 1999, the FDA approved GSK's prescription medication Avandia® (rosiglitazone) for the treatment of type 2 diabetes, "a serious and life threatening disease that affects about 18 to 20 million Americans." (Exh. 15, von Eschenbach Statement at 2; Compl. ¶ 23 (referring to von Eschenbach Statement).)[16] At the time of approval, there was no known concern about an increased risk for the cardiac ischemia that is the subject of the meta-analysis at issue in this action. GSK agreed to conduct a Phase 4 clinical study – the ADOPT trial – to further explore certain safety issues, including cardiovascular issues. (Exh. 16, FDA Briefing Document for Thiazolidinedione/Rosiglitazone Public Advisory Committee Meeting at 3 (dated 07/09/07), http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4308b1-02-fda-backgrounder.pdf (hereinafter "FDA Adv. Comm. Brief").) The FDA determined that "GSK diligently conducted [the ADOPT study] and fulfilled the regulatory requirement regarding the postmarketing commitment." (*Id.*)[17]

2. Post-Approval Clinical Trials

Since the FDA approved Avandia in 1999, GSK and others have conducted numerous clinical studies evaluating its use in patients with type 2 diabetes. (Exh. 16, FDA Adv. Comm. Brief at 3.) These studies have examined how well Avandia works "relative to other diabetes drugs individually and in combination" and "also shed new light on some of the safety

[16] "Diabetes is a leading cause of blindness, kidney failure, and limb amputation, and a major contributor to coronary heart disease." (Exh. 15, von Eschenbach Statement at 2-3.)

[17] The European Union ("EU") approved Avandia in July 2000. (*Id.* at 82.) As part of that approval, GSK agreed, *inter alia*, to conduct the RECORD trial, a cardiovascular mortality/morbidity study of six years duration with Avandia in combination with other anti-diabetic medications – either a sulfonylurea or metformin. (*Id.*) *See infra* Section II.B.2.c.

concerns associated with the product." (Exh. 15, von Eschenbach Statement at 3.) The FDA has "monitor[ed] several heart-related adverse events (e.g., fluid retention, edema, and congestive heart failure [CHF]) based on signals seen in these controlled clinical trials and from post-marketing reports." (*Id*.) To reflect these new data, the Agency updated Avandia's product labeling on several occasions. (*Id*.)[18]

In late 2006, the results from two large, long-term clinical trials involving Avandia – ADOPT and DREAM – were published in peer reviewed journals. In June 2007, interim results from the long-term RECORD trial were released. (*See, e.g.*, Compl. ¶¶ 29, 55-62; Exh. 40, Sarah Rubenstein, *Glaxo Letter Defends Avandia*, Wall St. J., May 31, 2007, at D6, *cited in* Compl. ¶ 34; Exh. 15, von Eschenbach Statement at 11-14; Exh. 17, FDA Background Introductory Memorandum for July 30, 2007 Advisory Committee Meeting at 5-6 (dated 07/09/07), http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4308b1-02-fda-backgrounder.pdf (hereinafter "FDA Adv. Comm. Intro. Mem."); Exh. 16, FDA Adv. Comm. Brief at 8-87.) As discussed below, none of these results showed a statistically significant cardiovascular risk with the use of Avandia. (*See, e.g.*, Exh. 15, von Eschenbach Statement at 11-14.)

[18] In April 2006, for example, the Agency updated Avandia's product labeling "to include new data in the WARNINGS section about a potential increase in heart attacks and heart-related chest pain in some patients." (Exh. 15, von Eschenbach Statement at 3.) The FDA based this labeling change on the results of a controlled clinical trial of patients with known, mild CHF in which "[a] higher number of heart attacks or angina was observed in patients treated with rosiglitazone compared to those treated with placebo." (*Id*.)

(a) The ADOPT Trial[19]

As explained above, GSK agreed to conduct the long-term, Phase 4 ADOPT trial at the time of the FDA's initial approval of Avandia in 1999. (*See supra* Section II.B.1; Exh. 16, FDA Adv. Comm. Brief at 3.) On December 4, 2006, GSK reported the results of the ADOPT trial. (Exh. 24, GSK Press Release, Landmark Study Shows Avandia® Is More Effective Than Metformin Or A Sulphonylurea In Long-Term Blood Sugar Control In Type 2 Diabetes (Dec. 4, 2006).)[20] On December 7, 2006, the results were published in *The New England Journal of Medicine*. (Exh. 36, Steven E. Kahn et al., *Glycemic Durability of Rosiglitazone, Metformin, or Glyburide Monotherapy*, 355 N. Engl. J. Med. 2427 (Dec. 7, 2006) (hereinafter "ADOPT Trial").)

The ADOPT trial's primary objective was to evaluate and compare the effects of long-term monotherapy of type 2 diabetes with Avandia and other anti-diabetic medications (glyburide/glibenclamide and metformin) on improvement and maintenance of glycemic control in over 4,350 patients with recently diagnosed diabetes. (Exh. 16, FDA Adv. Comm. Brief at 8.) The secondary objective included the assessment of cardiovascular safety. (*Id*.) Notably, the results of the ADOPT trial "do ***not*** support an increased ischemic risk of rosiglitazone relative to metformin or glyburide." (Exh. 15, von Eschenbach Statement at 11 (emphasis added); *see also* Exh. 16, FDA Adv. Comm. Brief at 76 ("Overall, ADOPT does not appear to present a

[19] The full title of the ADOPT trial is: "A Randomized, Double-Blind Study to Compare the Durability of Glucose Lowering and Preservation of Pancreatic Beta-Cell Function of Rosiglitazone Monotherapy Compared to Metformin or Glyburide/Glibenclamide in Subjects with Drug-Naïve, Recently Diagnosed Type 2 Diabetes Mellitus." (*See, e.g.*, Exh. 16, FDA Adv. Comm. Brief at 8.)

[20] GSK discussed the ADOPT results in other public disclosures as well. (*See, e.g.*, Exh. 25, GSK Press Release, Preliminary Results Announcement for the year ended 31st December 2006 (Feb. 8, 2007) at 2, *cited in* Compl. ¶ 58; Exh. 7, GSK Form 6-K (filed 2/8/07), at 2, *cited in* Compl. ¶¶ 58, 59; Exh. 11, GSK 2/8/07 Conf. Call Tr. at 9, *cited in* Compl. ¶ 60; Exh. 9, GSK 2006 Form 20-F (filed 03/02/07), at 31, *cited in* Compl. ¶ 62.)

significant signal of excess myocardial ischemic event risk, of excess total mortality, or of excess cardiovascular mortality for [Avandia] vs [glyburide/glibenclamide] or [metformin].").)[21]

(b) The DREAM Trial[22]

Researchers from the Population Health Research Institute at McMaster University conducted and analyzed the DREAM study. (*See* Exh. 16, FDA Adv. Comm. Brief at 77; Exh. 33, The DREAM Trial Investigators, *Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomized controlled trial*, 368 The Lancet 1096 (Sept. 15, 2006) (hereinafter "DREAM Trial").) This study was "a placebo-controlled, randomized, double-blind clinical trial in pre-diabetic patients designed to determine if the use of early treatment with medication could forestall the development of overt type 2 diabetes." (Exh. 15, von Eschenbach Statement at 12.)[23]

GSK announced the DREAM results on September 15, 2006. (Exh. 22, GSK Press Release, Avandia® (rosiglitazone maleate) Reduced Risk of Progression From Pre-Diabetes to Type 2 Diabetes by 62 Percent in Largest Completed Diabetes Prevention Trial; (Sept. 15, 2006).) The Company's press release described the results with respect to cardiovascular events:

> There was no significant difference between the rosiglitazone and placebo groups in withdrawal from study medication before study end, or in the secondary composite endpoint of cardiovascular (CV) events that included myocardial infarction, stroke, CV death,

[21] As the FDA has pointed out, "metformin is recommended by many treatment guidelines as the first line therapy for type 2 diabetes and has been shown in other long-term studies to lower cardiovascular risk." (Exh. 15, von Eschenbach Statement at 11.)

[22] The full title of the DREAM trial is "Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication." (*See, e.g.*, Exh. 16, FDA Adv. Comm. Brief at 77.)

[23] The study also "examined whether rosiglitazone and/or ramipril delayed onset of overt type 2 diabetes." (*Id.*) Nearly 5,300 patients participated in the trial. (*Id.*)

> confirmed heart failure, new angina and revascularization procedures (2.9 percent in the rosiglitazone group [75 events]; 2.1 percent in the placebo group [55 events], p=0.08). There was a low number of deaths in the trial and no significant difference between the two groups (1.1 percent in the rosiglitazone group [30 deaths] vs. 1.3 percent in the placebo group [33 deaths], p=0.7).

(*Id.* at 2.)[24] *The Lancet* published the results on-line the same day. (*See* Exh. 33, DREAM Trial at 1098.)

(c) The RECORD Trial[25]

The RECORD study was a post-marketing commitment to the European Medicines Evaluation Agency ("EMEA"). (*See supra* note 17; Exh. 15, von Eschenbach Statement at 13; Exh. 16, FDA Adv. Comm. Brief at 82.) The purpose of this trial, which is still ongoing, is to evaluate cardiovascular outcomes in over 4,400 patients with type 2 diabetes. (Exh. 15, von Eschenbach Statement at 13-14.) "[P]atients already receiving metformin were randomized to receive add-on rosiglitazone or sulfonylurea and patients already receiving sulfonylurea were randomized to receive add-on rosiglitazone or metformin." (*Id.*) The final results of the study, which was initiated in April 2001, are projected to be available in May 2009. (Exh. 16, FDA Adv. Comm. Brief at 82.)

After the publication of Dr. Nissen's meta-analysis, discussed below, an interim analysis of outcomes and deaths from cardiovascular causes collected at the time of randomization until March 30, 2007 was conducted in the RECORD trial. (Exh. 41, Philip D.

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[24] GSK discussed the DREAM results in other public disclosures as well. (*See, e.g.*, Exh. 23, GSK Press Release, Results announcement for the third quarter 2006 (Oct. 26, 2006) at 2, *cited in* Compl. ¶ 55; Exh. 3, GSK Form 6-K (filed 10/26/06), at 2, *cited in* Compl. ¶¶ 55; Exh. 10, GSK 10/26/06 Conf. Call Tr. at 7-8, *cited in* Compl. ¶ 56; Exh. 25, GSK Press Release, Preliminary Results Announcement for the year ended 31st December 2006 (Feb. 8, 2007) at 2, *cited in* Compl. ¶ 58; Exh. 7, GSK Form 6-K (filed 2/8/07), at 2, *cited in* Compl. ¶¶ 58, 59; Exh. 11, GSK 2/8/07 Conf. Call Tr. at 9, *cited in* Compl. ¶ 60; Exh. 9, GSK 2006 Form 20-F (filed 03/02/07), at 31, *cited in* Compl. ¶ 62.)

[25] The full name of the RECORD trial is "Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes." (*See, e.g.*, Exh. 16, FDA Adv. Comm. Brief at 82.)

Home, D.M., et al., *Rosiglitazone Evaluated for Cardiovascular Outcomes – An Interim Analysis*, 357 N. Engl. J. Med. 28, 29-30 (July 5, 2007) (available on-line June 5, 2007).) These interim results, which were published in the *New England Journal of Medicine* on-line on June 5, 2007, showed "no statistically significant differences between the rosiglitazone group and the control group regarding myocardial infarction and death from cardiovascular causes or any cause." (*Id*. at 1; *see also* Exh. 16, FDA Adv. Comm. Brief at 87 (explaining that "these results show no conclusive evidence that rosiglitazone has a statistically significant increase risk for ischemic events compared to metformin or sulfonylurea").)

3. GSK's Meta-Analysis

In or about December 2003, while the ADOPT, DREAM and RECORD trials were underway, the World Health Organization ("WHO") conducted an analysis of adverse reaction reports from the WHO Database that indicated a signal for increased cardiac risk (including both heart failure and ischemic events) for anti-diabetic medications, including Avandia, in the thiazolidinedione or "TZD" class. (*See* Exh. 17, FDA Background Introductory Memorandum for July 30 Advisory Committee Meeting (7/9/2007) ("FDA Adv. Comm. Intro. Mem.") at 4; Exh. 16, FDA Adv. Comm. Brief at 1.) While waiting for the results of the long-term cardiovascular outcomes trials, GSK sought to further evaluate Avandia's cardiovascular risk by conducting a statistical analysis ("pooled analysis" or "meta-analysis") of GSK-sponsored, randomized controlled clinical trials involving Avandia. (*See* Exh. 45, Results from Avandia Cardiovascular Event Modeling Project and Coronary Heart Disease Outcomes in Patients Receiving Antidiabetic Agents (posted on GSK's CTR on or about 10/27/06), http://ctr.gsk.co.uk/Summary/Rosiglitazone/III_CVmodeling.pdf (hereinafter "Results from GSK

Meta-Analysis and Balanced Cohort Study");[26] Exh. 17, FDA Adv. Comm. Intro. Mem. at 4; Exh. 16, FDA Adv. Comm. Brief at 1.)

In October 2005, GSK submitted summary information to the FDA "showing the preliminary results" of the Company's meta-analysis of data derived from the 37 Avandia clinical trials that had statistical analysis completed on or before September 30, 2004 (hereinafter "preliminary meta-analysis"),[27] and "proposed a formal analysis plan to provide a more definitive, formal examination of the pooled data" (Exh. 17, FDA Adv. Comm. Intro. Mem. at 4), which would include 5 additional clinical trials that had statistical analysis completed on or before August 2005, for a total of 42 trials (*see* Exh. 45, Results from GSK Meta-Analysis and Balanced Cohort Study at 1). In 2006, GSK completed its "more definitive, formal examination" of the meta-analysis of 42 randomized, controlled clinical trials involving the use of Avandia in patients with type 2 diabetes (hereinafter "final meta-analysis"), and submitted the final report of this analysis to the FDA in August 2006. (Exh. 17, FDA Adv. Comm. Intro. Mem. at 4; *see also* Exh. 15, von Eschenbach Statement at 3-4, 8; Exh. 16, FDA Adv. Comm. Brief at 1; Exh. 45, Results from GSK Meta-Analysis and Balanced Cohort Study.)[28]

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[26] As discussed in Section II.B.5, below, GSK posted the results from its meta-analysis on its publicly available Clinical Trial Register, which is accessible through the Company's website.

[27] Although plaintiffs refer to the 2005 meta-analysis as GSK's "***First*** Meta-Analysis," and the meta-analysis GSK submitted to the FDA in 2006 as GSK's "***Second*** Meta-Analysis" (*see, e.g.*, Compl. ¶¶ 25-26 (emphasis added)), the FDA considered the 2005 meta-analysis to be "preliminary" and the 2006 submission to be "a more definitive, formal examination of the pooled data" (*see* Exh. 17, FDA Adv. Comm. Intro. Memo. at 4).

[28] These 42 clinical trials were designed to assess the efficacy of Avandia for the treatment of Type 2 diabetes compared to either placebo or other anti-diabetic medications. The combined studies included 8,604 patients on Avandia and 5,633 patients on a variety of alternative therapeutic regimens, including placebo. (*See* Exh. 15, von Eschenbach Statement at 8.) As Commissioner von Eschenbach has explained:

> In general, these studies had differing primary efficacy endpoints; they were not designed to thoroughly investigate cardiovascular safety. Treatment groups varied and included rosiglitazone alone or in combination with insulin, sulfonylureas, and/or metformin. The comparator arms were varied and included placebo alone or as an add-on treatment to other anti-diabetic agents,

(continued...)

The final meta-analysis results "suggested an increased risk for myocardial ischemia." (Exh. 16, FDA Adv. Comm. Brief at 1.) Specifically, "the overall incidence of myocardial ischemia in rosiglitazone-treated subjects relative to the comparators was 1.99 percent vs. 1.51 percent with a hazard ratio of 1.31 (95 percent [confidence interval] 1.01.-1.70). This risk equates to a more than 30 percent excess risk of myocardial ischemic events in rosiglitazone-treated patients." (Exh. 15, von Eschenbach Statement at 9; *see also* Exh. 45, Results from GSK Meta-Analysis and Balanced Cohort Study.) In other words, "if this risk estimate were accurate and a patient's risk of having a heart attack in a given year were 2 percent, taking rosiglitazone would increase that risk to 2.6 percent. It does ***not*** mean that diabetics taking the drug have a 30 percent risk of having a heart attack." (Exh. 15, von Eschenbach Statement at 9 (emphasis in original).)

4. GSK's Balanced Cohort Study[29]

In addition to conducting the meta-analyses, described above, GSK commissioned a Balanced Cohort Study, an observational cohort study of 33,363 patients using a medical and pharmacy claims database. (*Id*. at 10; Exh. 17, FDA Adv. Comm. Intro. Mem. at 4.) As Dr. Garnier has explained in a *Wall Street Journal* article cited in the Complaint, GSK undertook this

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(continued...)

> and other active anti-diabetic treatment regimens. The combined patient population was diverse, including patients with average duration of diabetes ranging from 5 to 13 years as well as patients with significant risk factors for cardiovascular disease (e.g., history of myocardial infarction, bypass surgery, stroke, peripheral vascular disease, and New York Heart Association Class I and 2 heart failure). All but four studies were six month in duration or less.

(*Id*. at 8-9.)

[29] The full title of the Balance Cohort Study is "Coronary Heart Disease Outcomes in Patients Receiving Antidiabetic Agents." (*See* Exh. 17, FDA Adv. Comm. Intro. Mem. at 4; Exh. 45, Results from GSK Meta-Analysis and Balanced Cohort Study at 1.)

study "[a]s soon as [the Company] found out that there was at least a question raised by the meta-analysis." (Exh. 42, Jeanne Whalen, *Boss Talk: Glaxo's Garnier Is Taking the Heat – Defending Safety of Avandia Preoccupies, But Doesn't Consume, Drug Company's CEO,* Wall St. J., July 9, 2007, at B1 (hereinafter "Whalen article"), *cited in* Compl. ¶ 35.) GSK provided the final results of this Balanced Cohort Study to the FDA at the same time it submitted the completed meta-analysis. (Exh. 15, von Eschenbach Statement at 10.)[30]

Importantly, the findings from the Balanced Cohort Study "did ***not*** show an increased risk of adverse cardiovascular outcomes in patients taking rosiglitazone compared to other therapies." (*Id*. at 10-11 (emphasis added).) Specifically, "[t]he incidence of the composite cardiovascular endpoint was 1.75 events per 100 patient-years for the rosiglitazone-containing regimens and 1.76 events per 100 patient years for other treatments (hazard ratio 0.93; 95 percent CI 0.80-1.10)." (*Id*. at 10.) Thus, these findings "are inconsistent with the results of GSK's meta-analysis." (*Id*.)

The Complaint makes no mention of the Balanced Cohort Study or its results. (*See generally* Compl.) Yet, as explained in Section II.B.6, below, it was these conflicting results, and the fragility of the meta-analysis itself, that rendered the meta-analysis data

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[30] As the FDA has explained:

> The Balanced Cohort Study is an observational study of 33,363 patients using a medical and pharmacy claims database . . . . Propensity matching was used to match risk factors for cardiovascular disease and other considerations for patients initiating therapy. About 90 percent of the patients had no history of cardiovascular disease. The composite cardiovascular endpoint for the study was hospitalizations for myocardial infarction and coronary revascularization. Patients included in this study began treatment with rosiglitazone between the years 2000 and 2004. The treatment groups were monotherapy with rosiglitazone, metformin, or sulfonylurea; oral dual therapy (two-drug) combinations, and combinations that also included insulin. Follow up was 1.2 years.

(*Id*.)

inconclusive and "made it even more imperative that FDA examine all these data carefully and independently of the sponsor." (Exh. 15, von Eschenbach Statement at 11.)

5. Posting Of Meta-Analysis And Balanced Cohort Study Results On GSK's Clinical Trial Register

GSK submitted its final reports for the meta-analysis and Balanced Cohort Study to the FDA in August 2006.[31] (*See* Compl. ¶ 27; Exh. 15, von Eschenbach Statement at 3; Exh. 17, FDA Adv. Comm. Intro. Mem. at 4; Exh. 16, FDA Adv. Comm. Brief at 1.) On or before October 27, 2006, the Company posted both the meta-analysis results and the Balanced Cohort Study results on its CTR. (*See* Exh. 45, Results from GSK Meta-Analysis and Balanced Cohort Study). As discussed below, Dr. Nissen's data used for his meta-analysis was obtained from GSK's CTR and other publicly available sources. (*See* Exh. 37, Nissen Article.) Indeed, while "scrolling through" the CTR to gather data for his meta-analysis, Dr. Nissen reviewed GSK's meta-analysis and Balanced Cohort Study results that had been posted on the CTR. (Exh. 38, Anna Wilde Mathews, *Medical Detective – Sequel for Vioxx Critic: Attack on Diabetes Pill: Glaxo Shares Plunge as Dr. Nissen Sees Risk to Heart from Avandia*, Wall St. J., May 22, 2007, at A1.)

6. FDA's Evaluation Of GSK's Meta-Analysis And Cohort Study

The FDA found that GSK's meta-analysis and Balanced Cohort Study results "presented inconsistent data with regard to the potential cardiovascular risk of rosiglitazone."

[31] GSK also submitted the meta-analysis and Balanced Cohort Study to the EMEA. In September 2006, the EMEA revised the Summary of Product Characteristics and Package Leaflet for Avandia to include information on cardiovascular events. (*See* Exh. 30, EMEA, Avandia: Procedural steps taken and scientific information after authorisation at 2, http://www.emea.europa.eu/humandocs/PDFs/EPAR/Avandia/104300en8b.pdf; Exh. 27, EMEA Press Release, EMEA statement on recent publication on cardiac safety or rosiglitazone (May 23, 2007), http://www.emea.europa.eu/pdfs/general/direct/pr/23005707en.pdf; Exh. 39, Jean Whalen, *In Europe, Warning on Avandia is Old News*, Wall St. J., May 23. 2007, at 1; *see also* Exh. 31, EMEA, A Guideline on Summary of Product Characteristics (Oct. 2005), http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-2/c/spcguidrev1-oct2005.pdf.)

(Exh. 15, von Eschenbach Statement at 4.) Although GSK's meta-analysis observed an increased risk for myocardial ischemia, the Balanced Cohort Study "did not confirm a signal of concern associated with [Avandia] for the risk of [myocardial ischemia] or coronary revascularization relative to the other anti-diabetic therapies." (Exh. 16, FDA Adv. Comm. Brief at 1.) Moreover, "[i]n looking at all the studies to date related to the potential contribution of rosiglitazone to increasing the risk of heart attack," the FDA determined that the data were "inconsistent and conclusions [were] not clear." (Exh. 15, von Eschenbach Statement at 4.) Thus, "[g]iven the potential importance of the finding of excess risk of ischemic cardiovascular events, FDA decided to undertake its own meta-analysis to more fully evaluate this safety signal." (*Id*. at 10.) The FDA did not publicly discuss the meta-analysis and Balanced Cohort Studies when it received the data from GSK because the results were inconsistent and the Agency had begun a "comprehensive internal re-analysis" of the data. (*Id*. at 5, *paraphrased in* Compl. ¶ 27 (omitting full explanation).)

In ***April 2007***, the FDA conducted a "high level discussion of the issue of the cardiac safety of [rosiglitazone and another TZD, pioglitazone (Actos®)]." (Exh. 17, FDA Adv. Comm. Intro. Mem. at 5.) The FDA decided, *inter alia*, "to work on a communication strategy for alerting the public to [its] ongoing concerns and plans, above and beyond the data already in the rosiglitazone labeling on [cardiovascular] ischemic events." (*Id*. at 6.)

In addition, the Agency "planned to take both the issue of heart failure for both drugs [rosiglitazone and pioglitazone] and the [cardiovascular signal] to an Advisory Committee meeting in the ***late summer or early fall***." (*Id*. at 6 (emphasis added); *see also* Exh. 16, FDA Adv. Comm. Brief at 1.) The FDA intended to seek the Advisory Committee's expert advice as

to "how to interpret the large, often inconsistent dataset." (Exh. 15, von Eschenbach Statement at 7.)

On ***May 16, 2007***, the Agency met with GSK to discuss cardiovascular ischemic events with Avandia and "to see if they could provide other data or information that would better clarify or quantify the signal of risk." (Exh. 17, FDA Adv. Comm. Intro. Mem. at 6.)

On ***May 21, 2007***, the *New England Journal of Medicine* ("*NEJM*") published on-line the results of a separate meta-analysis of study level data from 42 clinical trials involving Avandia, conducted by Steven E. Nissen, M.D., and Kathy Wolski, M.P.H., of the Cleveland Clinic and based largely upon data provided on GSK's own website. (Compl. ¶ 32; *see also* Exh. 37, Nissen Article.) From their meta-analysis, Dr. Nissen and Ms. Wolski concluded that Avandia "was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes that had borderline significance." (*Id.* at 2457.)[32]

At the time of the *NEJM* publication, the FDA had not completed its re-analysis of the results of GSK's meta-analysis and Balanced Cohort Study. (Exh. 15, von Eschenbach Statement at 10.) With the release of the Nissen article, however, the Agency "accelerated it[s] public message about its ongoing work with regard to the [cardiovascular] signal and also moved

[32] On at least two occasions prior to the publication of this meta-analysis, Dr. Nissen had publicly expressed his concern with Avandia's cardiovascular safety based on publicly available data. On September 15, 2006, the day the DREAM study results were published, Dr. Nissen publicly opined that, although the increase in heart problems with Avandia was not statistically significant in the DREAM trial, "it still raise[d] concerns." (Exh. 34, Matthew Herper and Peter Kang, *Glaxo's Faustian Pill*, Forbes, September 15, 2006.) According to Dr. Nissen, "[t]he strong trend toward increased cardiovascular events is very troubling." (*Id*.) Dr. Nissen also publicly expressed his views after the ADOPT results were released on December 4, 2006. In an article released the same day, Nissen stated: "Because of the fact that adverse cardiovascular events went in the wrong direction in the [DREAM] trial and because they go in the wrong direction in this trial, I have concerns about the overall benefit of rosiglitazone in diabetic patients who are highly vulnerable to adverse cardiovascular outcomes, and this is not, in my opinion, a very favorable result. (Exh. 35, Amanda Gardner, New Type 2 Diabetes Drug Delays Disease Progression But Side Effects Include Cardiovascular Risks, Study Finds, Health Day, December 4, 2006.)

up the date for the Advisory Committee meeting, narrowing the focus of the meeting to the [cardiovascular] issue with rosiglitazone." (Exh. 17, FDA Adv. Comm. Intro. Mem. at 6.) As the FDA explained, it had "serious concerns that patients on Avandia and their health care providers [were] confused about the safety of this drug as a result of media reports surrounding the recent NEJM publication." (Exh. 15, von Eschenbach Statement at 7.)

Accordingly, on May 21, 2007, the same day the Nissen article was published on-line, the FDA issued a safety alert, which stated in pertinent part:

> The [FDA] is aware of a ***potential*** safety issue related to Avandia (rosiglitazone), a drug approved to treat type 2 diabetes. Safety data from controlled clinical trials have shown that there is a potentially significant increase in the risk of heart attack and heart-related deaths in patients taking Avandia***. However, other published and unpublished data from long-term clinical trials of Avandia, including an interim analysis of data from the RECORD trial (a large, ongoing, randomized open label trial) and unpublished reanalyses of data from DREAM (a previously conducted placebo-controlled, randomized trial) provide contradictory evidence about the risks in patients treated with Avandia.***
>
> . . . .
>
> ***FDA's analyses of all available data are ongoing. FDA has not confirmed the clinical significance of the reported increased risk in the context of other studies.*** Pending questions include whether the other approved treatment from the same class of drugs, pioglitazone, has less, the same or greater risks. Furthermore, there is inherent risk associated with switching patients with diabetes from one treatment to another even in the absence of specific risks associated with particular treatments. ***For these reasons, FDA is not asking GlaxoSmithKline, the drug's sponsor, to take any specific action at this time.*** FDA is providing this emerging information to prescribers so that they, and their patients, can make individualized treatment decisions.
>
> "FDA remains committed to assuring that doctors and patients have the latest information available to make treatment and medication use decisions. ***In this case, FDA is carefully weighing several complex sources of data, some of which show conflicting results, related to the risk of heart attack and heart-related deaths***

> ***in patients treated with Avandia***," said Steven Galson, M.D., M.P.H., director of FDA's Center for Drug Evaluation and Research. ***"We will complete our analyses and make the results available as soon as possible. FDA will take the issue of cardiovascular risk associated with Avandia and other drugs in this class to an Advisory Committee as soon as one can be convened."***

(Exh. 26, FDA Safety Alert (emphasis added), *cited in* Compl. ¶¶ 31, 65 (omitting most of text).)

On ***July 30, 2007***, the FDA convened a public Advisory Committee meeting, and asked the Committee, *inter alia*, "Does the overall risk-benefit profile of Avandia support its continued marketing in the US?," to which the Committee answered "yes" by a vote of 22 to 1. (*See* Summary Minutes of the joint meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee (approved Aug. 1, 2007), http://www.fda.gov/ohrms/dockets/ac/07/minutes/2007-4308m1-final.pdf.)[33] "The committee also advised that information warning of the potential for increased risk of heart attacks should be added to the drug labeling." (Exh. 28, FDA Press Release, FDA Adds Boxed Warning for Heart-related Risks to Anti-Diabetes Drug Avandia: Agency says drug to remain on market, while safety assessment continues (Nov. 14, 2007) (hereinafter "FDA Boxed Warning Press Release").)

On ***November 14, 2007***, the FDA and GSK each issued a press release, announcing that Avandia's labeling had been revised to include the following boxed warning:[34]

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[33] The transcript of the July 20, 2007 Advisory Committee Meeting, as well as the briefing documents submitted by GSK and FDA (including the portions of the FDA's Briefing Document that are appended hereto as Exhibit 16) are available on the FDA's website at http://www.fda.gov/ohrms/dockets/ac/cder07.htm#EndocrinologicMetabolic.

[34] A "boxed warning" in a label presents a contraindication or serious warning in a box that includes the word "warning" in uppercase letters. "The box must briefly explain the risk and refer to more detailed information in the 'Contraindications' or 'Warnings and Precautions' section" of the label. 21 C.F.R.§ 201.57(c)(1).

> A meta-analysis of 42 clinical studies (mean duration 6 months; 14,237 total patients), most of which compared Avandia to placebo, showed Avandia to be associated with an increased risk of myocardial ischemic events such as angina or myocardial infarction. Three other studies (mean duration 41 months; 14,067 patients), comparing Avandia to some other approved oral antidiabetic agents or placebo, have not confirmed or excluded this risk. ***In their entirety, the available data on the risk of myocardial ischemia are inconclusive***.

(*Id.* (emphasis added); *see also* Exh. 29, GSK Press Release, GlaxoSmithKline revises US labeling for Avandia® (Nov. 14, 2007) (hereinafter "GSK Boxed Warning Press Release").)

> The FDA's press release also explained:
>
> During the past year, FDA has carefully weighed several complex sources of data, some which show conflicting results, related to the risk of chest pain, heart attacks and heart-related deaths, and deaths from any cause in patients treated with Avandia.
>
> At this time, FDA has concluded that there isn't enough evidence to indicate that the risks of heart attacks or death are different between Avandia and some other oral type 2 diabetes treatments. Therefore, FDA has requested that GSK conduct a new long-term study to evaluate the potential cardiovascular risk of Avandia, compared to an active control agent. GSK has agreed to conduct the study and FDA will ensure it is initiated promptly.

(Exh. 28, FDA Boxed Warning Press Release.)

III. APPLICABLE PLEADING STANDARDS

A. To Avoid Dismissal Under *Bell Atlantic Corp. v. Twombly*, A Complaint Must Plead A Claim For Relief That Is Plausible On Its Face

To survive a motion to dismiss under Federal Rule of Civil Procedure 12(b)(6), a complaint must "allege *facts* that, accepted as true, make out the elements of a claim." *Sonds v. St. Barnabas Hosp. Corr. Health Servs.*, 151 F. Supp. 2d 303, 308 (S.D.N.Y. 2001) (emphasis added). A court "need not give 'credence to plaintiff's conclusory allegations' or legal conclusions offered as pleadings." *In re GlaxoSmithKline PLC Sec. Litig.*, No. 05-CV-3751,

2006 WL 2871968, at *5 (S.D.N.Y. Oct. 6, 2006) (quoting *Cantor Fitzgerald Inc. v. Lutnik*, 313 F.3d 704, 709 (2d Cir. 2002)).

Moreover, a complaint must plead a claim for relief "that is *plausible on its face*." *Bell Atlantic Corp. v. Twombly*, 127 S. Ct. 1955, 1974 (2007) (emphasis added) (abandoning standard from *Conley v. Gibson*, 355 U.S. 41, 45-46 (1957), that "a complaint should not be dismissed for failure to state a claim unless it appears beyond doubt that the plaintiff can prove no set of facts in support of his claim"); s*ee also Alexandra Global Master Fund, Ltd. v. Ikon Office Solutions, Inc.*, No. 06-CV-5383, 2007 WL 2077153, at *9 (S.D.N.Y. July 20, 2007) (dismissing Section 10(b) and Rule 10b-5 claim for failure to meet *Twombly* plausibility standard). Thus, factual allegations that fail "to raise a right to relief above the speculative level" or merely state a "conceivable" claim will not suffice. *Twombly*, 127 S. Ct. at 1974 (holding that complaint must be dismissed "[b]ecause the plaintiffs here have not nudged their claims across the line from conceivable to plausible"); *see also Gurfein v. Ameritrade, Inc.*, No. 04-CV-9526, 2007 WL 2049771, at *1 (S.D.N.Y. July 17, 2007) (Stanton, J.) (applying *Twombly* plausibility standard to federal securities claims).

B. Federal Rule Of Civil Procedure 9(b) And The Private Securities Litigation Reform Act Impose Heightened Pleading Standards On Securities Fraud Claims

In addition to meeting the *Twombly* plausibility standard, a complaint alleging securities fraud under Section 10(b) and Rule 10b-5 must satisfy the heightened pleading requirements mandated by Federal Rule of Civil Procedure 9(b) and the Private Securities Litigation Reform Act of 1995 ("PSLRA"), 15 U.S.C. § 78u-4(b) (2007). Rule 9(b) requires that "[i]n all averments of fraud or mistake, the circumstances constituting fraud or mistake . . . be stated with particularity." Fed. R. Civ. P. 9(b). *See also Ross v. A. H. Robins Co., Inc.*, 607 F.2d 545, 557 (2d Cir. 1979) (to protect defendant from undue harm to its reputation, allegations of

fraud must be plead with particularity). Accordingly, a complaint must "(1) specify the statements that the plaintiff contends were fraudulent, (2) identify the speaker, (3) state where and when the statements were made, and (4) explain why the statements were fraudulent." *Novak v. Kasaks*, 216 F.3d 300, 306 (2d Cir. 2000) (quoting *Shields v. Citytrust Bancorp, Inc.*, 25 F.3d 1124, 1128 (2d Cir. 1994)). Mere conclusory allegations unsupported by facts do not suffice. *See Luce v. Edelstein*, 802 F.2d 49, 54 (2d Cir. 1986).

Congress enacted the PSLRA in 1995 for the specific purpose of curbing Rule 10b-5 litigation abuses, such as "nuisance filings, targeting of deep-pocket defendants, vexatious discovery requests and manipulation by class action lawyers," *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 127 S. Ct. 2499, 2508 (2007) (quoting *Merrill Lynch, Pierce, Fenner & Smith, Inc. v. Dabit*, 547 U.S. 71, 81 (2006)), which reportedly "resulted in extortionate settlements, chilled any discussion of issuers' future prospects, and deterred qualified individuals from serving on boards of directors," *Dabit*, 547 U.S. at 81 (quoting H.R. Rep. No. 104-369, at 31-32 (1995)). The PSLRA attempts to control these abuses by, *inter alia*, imposing "[e]xacting pleading requirements" on Rule 10b-5 plaintiffs. *Tellabs*, 127 S. Ct. at 2504. Specifically, the PSLRA requires plaintiffs to "specify each statement alleged to have been misleading, the reason or reasons why the statement is misleading, and, if an allegation regarding the statement or omission is made on information and belief, the complaint shall state with particularity all facts on which that belief is formed." 15 U.S.C. § 78u-4(b)(1) (2007).

The PSLRA also mandates that a plaintiff "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind." 15 U.S.C. § 78u-4(b)(2) (2007). For Rule 10b-5 actions, the required state of mind is scienter – "the defendant's intention 'to deceive, manipulate, or defraud.'" *Tellabs*, 127 S. Ct. at 2504 (quoting

Ernst & Ernst v. Hochfelder, 425 U.S. 185, 194, n.12 (1976), and citing 15 U.S.C. § 78u-4(b)(1), (2) (2007)); *see also ATSI Commc'ns, Inc. v. Shaar Fund, Ltd.*, 493 F.3d 87, 99 (2d Cir. 2007). "For an inference of scienter to be strong, 'a reasonable person must deem it cogent and at least as compelling as any opposing inference one could draw from the facts alleged.'" *ATSI Commc'ns*, 493 F.3d at 99 (quoting *Tellabs*, 127 S. Ct. at 2510). Where, as here, a complaint fails to comply with the PSLRA's heightened pleading requirements, "the court *shall*, on the motion of any defendant, dismiss the complaint . . . ." 15 U.S.C. § 78u-4(b)(3)(A) (2007) (emphasis added).

C. The Court May Properly Consider Certain Documents Not Attached To The Complaint When Determining Whether Plaintiffs' Claims Meet The Applicable Pleading Requirements

In assessing whether a complaint complies with the applicable pleading requirements, including whether a strong inference of scienter has been raised, the Court properly may look beyond the four corners of the Complaint. Indeed, as the Supreme Court recently acknowledged in *Tellabs*, for purposes of weighing competing inferences, the Court should consider as well documents attached to the complaint as exhibits, incorporated by reference, or "integral to the complaint." *Tellabs*, 127 S. Ct. at 2509; *see also Roth v. Jennings*, 489 F.3d 499, 509 (2d Cir. 2007) (permitting the attachment of documents filed with the SEC "because no serious question as to their authenticity can exist"); *Gurfein v. Ameritrade*, No. 04 Civ. 9526, 2007 WL 2049771, at *1 (S.D.N.Y. July 17, 2007) (Stanton, J.). Notably, plaintiffs may not avoid the effect of this rule merely by failing to attach or identify documents on which they obviously relied.[35]

[35] Here, plaintiffs allege that their claims are based upon, *inter alia*, "a review of the public documents and announcements concerning [GSK], [SEC] filings, wire and press releases published by and regarding [GSK], and information readily available on the Internet." (Compl. at p. 1.) The Complaint specifically cites, quotes,

(continued...)

The Court also may consider documents of which judicial notice can be taken, such as documents that are required by law to be filed, and were filed, with a government agency such as the SEC. *See, e.g., Kramer v. Time Warner Inc.* 937 F.2d 767, 774 (2d Cir. 1989) ("[A] district court may take judicial notice of the contents of relevant public disclosure documents required to be filed with the SEC as facts 'capable of accurate and ready determination by resort to sources whose accuracy cannot reasonably be questioned.'"). The Court may take judicial notice of publicly available documents issued by government agencies, including the U.S. Food and Drug Administration ("FDA"). *See, e.g., In re Merck & Co., Inc. Sec., Derivative & "Erisa" Litig.*, 483 F. Supp. 2d 407, 419 n.2 (D.N.J. 2007) (noting that court may properly consider FDA Warning Letter when deciding motion to dismiss); *Noble Asset Mgmt. v. Allos Therapeutics, Inc.*, No. 04-CV-1030, 2005 WL 4161977, at *2 (D. Colo. Oct. 20, 2005) (denying plaintiff's motion to strike FDA guidance documents, reasoning that such public documents related to FDA's "process for reviewing new drug applications and that process is central to an evaluation of the claims made in this case"); *In re Wellbutrin SR/Zyban Antitrust Litig.*, 281 F. Supp. 2d 751, 754-55 n.2 (E.D. Pa. 2003) (taking judicial notice of FDA's published reports, posted on its website); *DeMarco v. DepoTech Corp.*, 149 F. Supp. 2d 1212, 1218 (S.D. Cal. 2001) (recognizing that, on motion to dismiss, a court may properly consider transcript of FDA advisory committee meeting).[36] The Court may take judicial notice of news articles, *In re eSpeed, Inc. Sec. Litig.*, 457 F. Supp. 2d 266, 277 (S.D.N.Y. 2006), as well as information posted

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(continued...)

paraphrases and/or refers to statements set forth in Exhibits 1-11, 15, 18-21, 23, 25-26, 37, 40, 42, and 46(a-c) in the accompanying Appendix.

[36] Defendants respectfully ask that the Court take judicial notice of Exhibits 12-14, 16-17, 22, 24, 27-31, 33-36, 38-39, 41, 43–45 in the accompanying Appendix.

on a party's website, *Doron Precision Sys., Inc. v. FACC, Inc.*, 423 F. Supp. 2d 173, 179 n.8 (S.D.N.Y. 2006).

Finally, "[t]he Court need not accept as true any allegations that are contradicted by documents deemed to be part of the complaint, or materials amenable to judicial notice." *In re Yukos Oil Co. Sec. Litig.*, No. 04-CV-5243, 2006 WL 3026024, at *12 (S.D.N.Y. Oct. 25, 2006); *accord In re Aegon N.V. Sec. Litig.*, No. 03-CV-0603, 2004 WL 1415973, at *5 (S.D.N.Y. June 23, 2004); *Rapoport v. Asia Elecs. Holding Co.*, 88 F. Supp. 2d 179, 184 (S.D.N.Y. 2000); *In re Hunter Envtl. Servs. Inc. Sec. Litig.*, 921 F. Supp. 914, 918-19 (D. Conn. 1996).

IV. ARGUMENT

To state a claim under Section 10(b)[37] and Rule 10b-5,[38] a plaintiff must plead that, "'in connection with the purchase or sale of securities, the defendant, acting with scienter, made a false material misrepresentation or omitted to disclose material information, and that plaintiff's reliance on defendant's action caused [plaintiff's] injury.'" *In re Time Warner Inc. Sec. Litig.*, 9 F.3d 259, 264 (2d Cir. 1993) (quotation omitted) (alteration in original). Accordingly, plaintiffs must allege with particularity each of the following essential elements: (1) a material misrepresentation or omission; (2) scienter; (3) a connection with the purchase or

[37] Section 10(b) prohibits the "use or employ[ment], in connection with the purchase or sale of any security, . . . [of] any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the [SEC] may prescribe . . . ." 15 U.S.C. § 78j(b) (2007).

[38] Rule 10b-5 specifically provides that it is unlawful to "make any untrue statement of a material fact or to omit to state a material fact necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading . . . in connection with the purchase or sale of any security." 17 C.F.R. § 240.10b-5.

sale of a security; (4) reliance; (5) economic loss; and (6) loss causation. *See, e.g.*, *Dura Pharmaceuticals, Inc. v. Broudo*, 544 U.S. 336, 341-42 (2005).

The failure to adequately plead any one of these essential elements necessarily precludes a securities fraud claim. Thus, for each of the following separate and independent reasons, plaintiffs' Complaint fails to state a Rule 10b-5 claim and must be dismissed.

A. Plaintiffs Have Not Alleged Any Materially False Or Misleading Statement Or Misleading Omission

Plaintiffs do not allege that defendants made any false statements of fact. Nor do they aver that defendants misrepresented any hard facts, engaged in accounting irregularities or "cooked the books." Instead, the ***sole*** basis for plaintiffs' Rule 10b-5 claim is their contention that several otherwise accurate statements regarding increased sales of Avandia, opinions regarding the future prospects of Avandia, and disclosures reporting the results of certain long term studies of Avandia were rendered materially misleading by the absence of any reference to GSK's meta-analysis regarding Avandia's cardiovascular safety. But, as the Complaint concedes, the FDA itself considers the meta-analysis results to be inconclusive when viewed in context of the entirety of the available data regarding Avandia's cardiovascular risk. As explained below, a pharmaceutical company has no duty to disclose safety information under such circumstances.

1. Plaintiffs Do Not Claim That Defendants Made Any Factual Misstatements, And Instead Rely Solely On A Theory Of Fraud By Omission

Plaintiffs have not identified a single factual inaccuracy in any statement by any defendant during the putative Class Period. Instead, plaintiffs challenge statements that are either factually accurate on their face, or simply projections of future sales of Avandia. In paragraphs 42, 45, 46, 47, and 49, for example, plaintiffs cite statements made in press releases,

conference calls with investors and analysts, and annual reports regarding the past and projected future success of Avandia between the time GSK completed the preliminary meta-analysis and when it completed the final meta-analysis that are nothing more than statements of historical fact and opinions about how Avandia may perform in 2006.[39] Plaintiffs do not allege that any of these statements is factually inaccurate, and nowhere do plaintiffs assert that Avandia was ***not*** a key growth driver in 2005 and 2006. Rather, the ***only*** theory plaintiffs offer as to why these statements are actionable is that they supposedly "were materially false and misleading because they failed to disclose that the Company had completed the First Meta-Analysis [preliminary meta-analysis], which showed a risk of heart attack linked to the use of Avandia." (Compl. ¶ 43.) Plaintiffs allege that "the positive statements made about Avandia and its contribution to the Company's financial results created an obligation to disclose the then-known adverse facts concerning the risks and safety issues attendant to the use of Avandia." (*Id.*)

Similarly, plaintiffs take issue with several statements about Avandia's past and projected future performance that were made after GSK finalized its meta-analysis.[40] Again,

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[39] Plaintiffs take issue with statements such as:

• "This quarter's performance shows the vitality of our business, which is again being driven by great performances from key products such as … Avandia…" (Compl. ¶ 42 (citing Exh. 1, GSK Form 6-K (filed 10/27/05), at 3).)

• "Looking into 2006, the strong growth seen from key products such as Seretide/Advair, Avandia and from our vaccines business is set to continue…" (*Id.* ¶ 46 (citing Exh. 19, GSK Press Release, Preliminary Announcement of Results for the year ended 31st December 2005 (Feb. 8, 2006) at 1).)

• "We still see Advair, Seretide, and Avandia as well as our vaccine portfolio as significant growth drivers." (*Id.* ¶ 47 (citing Exh. 11, GSK, 2/8/06 Conf. Call Tr. at 8).)

• "Looking into 2006, the strong growth seen from key products [including Avandia] and from our vaccines business is expected to continue….." (Id. ¶ 49 (citing Exh. 2, GSK 2006 Form 20-F (filed 3/3/06), at 71).)

[40] Plaintiffs challenge the following statements:

• "Sales growth of existing products and launch of new products are key drivers of GSK's business performance. The strong growth seen from key products such as Seretide/Advair, Avandia/Avandamet and from

(continued...)

plaintiffs do not allege that these statements are anything other than factually accurate statements of financial performance or opinions about the future prospects of Avandia. Rather, plaintiffs rely solely on absence of any discussion of GSK's meta-analysis as the reason why these statements are false and materially misleading. (*See id*. ¶¶ 50, 52, 54, 57, 63.)

Finally, plaintiffs point to several statements regarding the results of the DREAM and ADOPT studies. Most of the statements cited by plaintiffs,[41] however, discussed the efficacy results of the studies, not any issue related to cardiovascular safety. (*See id*. ¶ 56 (citing

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(continued...)

GSK's vaccines business is expected to continue." (*Id.* ¶ 49 (citing Exh. 2, GSK 2006 Form 20-F (filed 3/3/06), at 1).)

- "For the first quarter of 2006, the Company reported earnings of 26.5p per share, up from 21.1p per share for the first quarter of 2005. In the press release, Avandia was called one of the Company's 'key growth drivers.'" (*Id*. ¶ 51 (citing Exh. 20, GSK Press Release, Results announcement of for the first quarter 2006 (April 27, 2006) at 2).)

- "For the second quarter, the Company reported earnings of 23.3p per share, up from 20.4p per share for the second quarter of 2005. Defendant Garnier, in "commenting on the performance in the quarter and GSK's outlook" attributed the Company's ability 'to raise our earnings guidance' for 2006 to pharmaceutical sales growth, including a 32% increase in sales of Avandia." (*Id*. ¶ 53 (citing Exh. 21, GSK Press Release, Results announcement for the second quarter 2006 (July 26, 2006) at 1)).)

- "For the third quarter, the Company reported earnings of 24.7p per share, up from 21.3p per share for the third quarter of 2005. The press release specifically highlighted the contributions that Avandia was making to the Company's financial results, stating: 'The Avandia family of products, for the treatment of type 2 diabetes, continues to perform well with sales up 11% to £378 million in the quarter.'" (*Id*. ¶ 55 (citing Exh. 23, GSK Press Release, Results announcement for the third quarter 2006 (Oct. 26, 2006) at 1).)

- "Sales growth of existing products and launch of new products are key drivers of GSK's business performance. The strong growth seen from key products such as. . .Avandia. . . is expected to continue in 2007." (*Id*. ¶ 62; Exh. 9, GSK 2007 Form 20-F (filed 3/2/07), at 1.)

[41] In paragraph 29 of the Complaint plaintiffs allege – without citation – that "at the same time Defendants were aware of the conclusions from their own meta-analyses, they repeatedly highlighted studies which, according to Defendants, demonstrated that Avandia showed (or will show) no increase in myocardial infarctions or cardiovascular-related death." (Compl. ¶ 29.) Notably, none of the statements upon which the Complaint actually relies supports this broad assertion. Rather, almost all of the statements about the DREAM and ADOPT studies cited by plaintiff focused on the efficacy of Avandia, not its safety.

Exh. 10, GSK 10/26/06 Conf. Call Tr. at 11); ¶ 60 (citing Exh. 11, GSK 2/8/07 Conf. Call Tr. at 9).)[42] There is no allegation that defendants inaccurately described the data from the DREAM or ADOPT study. There is no dispute, for example, that the data from DREAM showed, in fact, that "Avandia can reduce the risk of progression to type 2 diabetes" or that in the ADOPT study Avandia "tied [metformin] on the cardiovascular safety."[43] The hard data was publicly disclosed in medical journals, and the scientific and investment communities were free to, and did, interpret the data for themselves. (*See* Exh. 33, DREAM Trial; Exh. 36, ADOPT Trial.)[44] The only theory offered by plaintiffs as to why these statements were rendered misleading is that the discussion of the "positive results" from the studies "created an obligation to disclose the adverse information from the First Meta-Analysis [preliminary meta-analysis] and Second Meta-Analysis [completed meta-analysis]." (Compl. ¶ 57; *see also id.* ¶ 61.)

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[42] The investment community was free to interpret the publicly available data from the ADOPT study, so Mr. Stout's general commentary that the study's results were "[e]xtremely excit[ing]" is hardly the kind of statement upon which reasonable investors would rely in making investment decisions. "[A]nalysts and investors rely on ***facts*** in making investment decisions, not vague expressions of corporate optimism or competitive strengths." *In re: Fleming Companies, Inc., Sec. & Derivative Litig.*, No. CIVA 503MD1530TJW, MDL-1530, 2004 WL 5278716, at *26 (E.D. Tex. Jun. 16, 2004) (emphasis in original) (citing *Rosenzweig v. Azurix Corp.*, 332 F.3d 854, 869-70 (5th Cir. 2003)).

Indeed, most of the statements plaintiffs challenge are simply the kind of vague "puffing" that courts regularly find not actionable as a matter of law. (*See, e.g.*, Compl. ¶ 42 ("This quarter's performance shows the vitality of our business, which is again being driven by great performances from key products such as . . . Avandia . . . ."); Compl. ¶ 44 ("Obviously we've had tremendous success with Avandia. . . . . [W]e don't expect the growth rate to slow down over the next couple years."); Compl. ¶ 49 (describing Avandia as a "key product")). "[E]xpressions of corporate puffery and corporate optimism do not give rise to securities violations." *Rombach v. Chang*, 355 F.3d 164, 174 (2d Cir. 2004); *see also Leykin v. AT&T Corp.*, 423 F. Supp. 2d 229, 247 (S.D.N.Y. 2006) (Stanton, J.) (finding statements of chief financial officer non-actionable because of their "vagueness and generality"). "The corporate puffery rule applies to both loose optimism about both a company's current state of affairs and its future prospects." *In re Nokia Oyj (Nokia Corp.) Sec. Litig.*, 423 F. Supp. 2d 364, 397 (S.D.N.Y. 2006) (citing *Fitzer v. Sec. Dynamics Tech., Inc.*, 119 F. Supp. 2d. 12, 23 (D. Mass. 2000)).

[43] Indeed, in a release to health care providers issued by the FDA in May 2007, it confirmed that the ADOPT "data do not support an ischemic risk of rosiglitazone relative to metformin." (Exh. 18 [May 2005 Information for Healthcare Professionals Release from FDA].)

[44] *See supra* n. 33 (discussing Dr. Nissen's concerns with results of DREAM and ADOPT results).)

Thus, all of plaintiffs' claims boil down to one, ultimately insupportable contention – that defendants committed securities fraud by failing to disclose the meta-analysis results. But, as explained below, there was no such duty as a matter of law.

2. Plaintiffs Have Failed To Plead Any Facts Showing That Defendants Had A Duty To Disclose The Meta-Analyses

"Silence, absent a duty to disclose, is not misleading under Rule 10b-5." *Basic Inc. v. Levinson*, 485 U.S. 224, 229 n. 17 (1988). Rather, a "duty to disclose may arise when there is insider trading, a statute requiring disclosure, or an inaccurate, incomplete or misleading prior disclosure." *Oran v. Stafford*, 226 F.3d 275, 285-86 (3d Cir. 2000); *Glazer v. Formica Corp.*, 964 F.2d 149, 152 (2d Cir. 1992). Thus, the securities laws do not require corporations to make constant disclosures as they continue to analyze data regarding their products. As the Second Circuit has explained, "[c]ompanies conduct many experiments and test in connection with their products, and to require the public announcement of each one would risk 'burying the shareholders in an avalanche of trivial information.'" *San Leandro Emergency Med. Group Profit Sharing Plan v. Philip Morris Co.*, 75 F.3d 801, 810 (2d Cir. 1996) (quoting *TSC Indus., Inc. v. Northway, Inc.*, 426 U.S. 438, 448 (1976)).

It is well settled that pharmaceutical manufacturers are under no duty to disclose safety data regarding a product until there is reason to believe that the future viability of the product is jeopardized. *See, e.g., In re Carter-Wallace, Inc. Sec. Litig.*, 150 F.3d 153, 157 (2d Cir. 1998) (*Carter-Wallace I*); *Oran*, 226 F. 3d at 285; *In re Bayer AG Sec. Litig.*, No. 03-CV-1546, 2004 WL 2190357 (S.D.N.Y. Sept. 30, 2004); *In re Intrabiotics Pharm. Inc. Sec. Litig.*, No. C 04-02675, 2006 WL 2192109 at **12-15 (N.D. Cal. Aug. 1, 2006); *see also In re Alliance Pharm. Corp. Sec. Litig.*, 279 F. Supp. 2d 171, 189 (S.D.N.Y. 2003) ("The Second Circuit thus implicitly recognized that not every adverse effect in a clinical trial is automatically material, and

that causation, as well as statistical significance, is key."). This rule is based on the fact that pharmaceutical companies regularly review data concerning their products, and data indicating a potential safety issue may be "random and may not establish a nexus between a drug and the reported illness." *In re Bayer AG Sec. Litig.*, 2004 WL 2190357, at *9. In the absence of hard evidence establishing that a link between the medication and the safety issue does, in fact, exist, disclosure is premature. "[U]ntil a connection between [a drug] and any illness could be made, we would not expect [a drug manufacturer] to abandon its product on what, at the time, would have been speculation." *In re Carter-Wallace, Inc. Sec. Litig.*, 220 F.3d 36, 42 (2d Cir. 2000)("*Carter-Wallace II*").

In *Carter-Wallace I*, the plaintiffs alleged that the manufacturer of Felbatol, an anti-epileptic medication, committed securities fraud when the manufacturer failed to disclose a number of "adverse event reports" suggesting that patients taking Felbatol had suffered a fatal form of bone marrow disease. *Carter-Wallace I*, 150 F.3d at 155. The plaintiffs claimed that certain statements in the company's financial statements that reported positive sales trends and royalties of Felbatol were rendered materially misleading by the failure to disclose the adverse event reports. *Id.* at 157. The Second Circuit affirmed the district court's dismissal of this portion of the claim,[45] finding that there was no duty to disclose the adverse event reports prior to August 1, 1994 – the date the manufacturer and the FDA issued a joint "Dear Doctor" letter, recommending that most patients be withdrawn from the medication. *Id.* at 155-57. The court reasoned:

> The statements in Carter-Wallace's Form 10-K and its "Report to Shareholders" did not become materially misleading until Carter-

[45] Another portion of the claim was remanded to the district court on a different issue, and the Second Circuit subsequently affirmed the dismissal of all claims in *Carter-Wallace II*, 220 F.3d 36 (2d Cir. 2000).

> Wallace had information that Felbatol had caused a statistically significant number of aplastic-anemia deaths and therefore had reason to believe that the commercial viability of Felbatol was threatened. ***Drug companies need not disclose isolated reports of illness suffered by users of their drugs until those reports provide statistically significant evidence that the ill effects may be caused by – rather than randomly associated with – use of the drugs and are sufficiently serious and frequent to affect future earnings.***

Id. at 157 (emphasis added); *accord Oran*, 226 F.3d at 283-84 (finding that there was no duty to disclose certain data regarding the safety of the diet drug "Fen-Phen" that was not statistically significant and did not conclusively establish a safety problem); *In re Intrabiotics Pharm.*, 2006 WL 2192109 at *14 (citing *Carter-Wallace* for the proposition that "'[d]rug companies need not disclose isolated reports of illnesses suffered by users of their drugs until those reports provide statistically significant evidence that ill effects may be caused by – rather than randomly associated with – use of the drugs and are sufficiently serious and frequent to affect future earnings'") (quoting *Carter-Wallace I*, 150 F.3d at 157).

In *In re Bayer AG Securities Litigation*, the plaintiffs brought a securities fraud claim against Bayer relating to the withdrawal of "Baycol" due to concerns that it caused rhabdomyolysis – a muscular disorder. 2004 WL 2190357, at *6. Plaintiffs alleged that various positive statements about Baycol were misleading because Bayer failed to disclose a wealth of safety data relating to use of the medication. *Id.* at *2. The Complaint alleged a detailed, fact laden chronology of increasing concerns within Bayer about the safety profile of Baycol, including the following:

- In July 1997, Bayer received a letter from its marketing partner, SmithKline Beecham "expressing serious concerns over possible drug interactions with Baycol and warning that '[s]imple and safe no longer appear to be a viable promotion platform.'" *Id.* at *2.
- "By April 23, 1999, Bayer's safety department had received fifty-one adverse event reports of Baycol related rhabdomyolysis in the United States." *Id.* at *3.

- "In October 1999, Bayer's senior drug safety officer in the United States reported by email that the incidence of myopathy among patients taking Baycol in tandem with [another drug] had increased 'about 60%.'" *Id.*

- "By the end of 1999, adverse event reports were inundating Bayer. . . . An internal memorandum for senior Bayer executives dated December 30, 1999 reported that . . . '[t]he steadily increasing numbers of spontaneous reports of rhabdomyolysis associated with Baycol, along with additional telephone activity, have overwhelmed the available Safety Assurance resources . . . .'" *Id.* at *4.

- "On March 10, 2000, Dr. Steve Niemcryk, an epidemiologist in Bayer's Safety Surveillance group, notified Bayer's Scientific Relations department that adverse event reports disclosed that the risk of rhabdomyolysis with Baycol was between five and 67 times greater than with other [drugs in the same class]. . . . Niemcryk cautioned that his findings needed to be evaluated with care because adverse event reports are of questionable reliability. . . ." *Id.*

Despite the specificity of the pleading, relying on *Carter-Wallace I*, the *Bayer* court found that the manufacturer was under no duty to disclose any of this information. Rather, a duty to disclose arose only after an August 2, 2000 meeting, when "senior members of Bayer's Global Drug Safety team and consultants met . . . to discuss the accumulation of adverse event reports [and] a consensus emerged that the data concerning Baycol's dangers 'was putting the brand at risk.'" *Id.* at *5, **8-9. (citation omitted).

> Construing all inferences in plaintiffs' favor, by August 2000, defendants viewed the adverse event reports as 'sufficiently serious and frequent to affect future earnings.' *Carter-Wallace I*, 150 F.3d at 157. Thus, defendants were obligated at that time to update their pre-withdrawal statements concerning Baycol's safety profile. . . . While defendants were under a duty to disclose the adverse event data after August 2000, no such duty arose prior to that time. ***The adverse event reports and other documents were not material before the August 2000 safety conference***.

Id. at *10 (emphasis added).

Here, plaintiffs have alleged ***no*** facts – never mind facts pleaded with the particularity required by Rule 9(b) and the PSLRA – which establish that there was any

significant reason to believe that the future viability of Avandia was jeopardized prior to May 21, 2007. All the Complaint alleges, in the most conclusory of terms, is that the meta-analyses showed that Avandia is "***associated***" with an increased risk of heart attack. (*See* Compl. ¶ 25 (alleging that "Glaxo's First Meta-Analysis [preliminary meta-analysis] showed an estimate of excess risk of ischemic cardiovascular events, *i.e.*, an increased risk of heart attack, ***associated*** with the use of Avandia." (emphasis added); Compl. ¶ 26 ("Glaxo's Second Meta-Analysis [completed meta-analysis] showed an estimate of excess risk of ischemic cardiovascular events ***associated*** with the use of Avandia that was even greater than the risk portrayed in the First Meta-Analysis [preliminary meta-analysis]." (emphasis added)); Compl. ¶ 28 ("Despite knowing that the data of the Company's meta-analysis showed an increased risk of heart attacks ***associated*** with the use of Avandia, Defendants did not disclose this material information to investors during the Class Period." (emphasis added)).)

Indeed, the documents upon which plaintiffs rely actually show that the meta-analyses conducted by GSK were not reliable in light of other available data. Even the Nissen study cited by plaintiffs acknowledges that: "A meta-analysis is always considered less convincing than a large prospective trial designed to assess the outcome of interest." (Exh. 37, Nissen Article at 2469.) Moreover, meta-analysis as a methodology has serious limitations, as the FDA has acknowledged,[46] and is particularly unreliable where, as here, its results conflict with that of far more reliable studies such as long-term, randomized controlled clinical trials. Thus, the meta-analysis results alone cannot clear the *Carter-Wallace* hurdle.

Moreover, as plaintiffs themselves admit, GSK ***promptly disclosed to the FDA*** the very data plaintiffs claim the Company fraudulently concealed from investors. (Compl.

[46] *See supra* n. 7.

¶ 27.) And plaintiffs acknowledge that, although the FDA had the data for months, the Agency determined that the data should ***not*** be publicly disclosed before the FDA had performed "a comprehensive internal re-analysis of the data." (*Id*.)

Furthermore, documents referenced in the Complaint demonstrate unequivocally that the FDA had difficulty drawing any significant conclusions based on GSK's meta-analyses. In his June 6, 2007 statement before the United States House of Representatives' Committee on Oversight and Government Reform, FDA Commissioner von Eschenbach explained the reasons the Agency did not publicly discuss the data:

> In August 2006, the manufacturer of Avandia, GlaxoSmithKline (GSK or the company), provided FDA with a pooled analysis (meta-analysis) of 42 separate double blinded, randomized, controlled clinical trials to assess the efficacy of rosiglitazone for treatment of type 2 diabetes compared to either placebo or other anti-diabetic therapies in patients with type 2 diabetes. ***At the same time, the company also provided a population-based database study discussed below. The pooled analysis and the population-based database study presented inconsistent data with regard to the potential cardiovascular risk of rosiglitazone.***[47] Since then, results of other long-term controlled clinical studies have been published or unpublished results have been made available to FDA. ***In looking at all the studies to date related to the potential contribution of rosiglitazone to increasing the risk of heart attack, the data are inconsistent and conclusions are not clear.***
>
> * * *
>
> Let me describe FDA's public communication about the data related to risk for heart attacks. FDA did not publicly discuss the data submitted by GSK at the time it was submitted in August 2006, ***because the data from the pooled analysis and the***

[47] The first sentence of Paragraph 27 of the Complaint is taken almost verbatim from Commissioner von Eschenbach's statement to Congress. The plaintiffs then omit this next sentence, which points out that GSK had performed the Balanced Cohort Study, which showed no increase risk of heart attacks.

> ***population based study were inconsistent***[48] and we began a comprehensive re-analysis of those data.

(Exh. 15, von Eschenbach Statement at 3-5; *see also* Compl. ¶ 27.)

Thus, despite the fact that plaintiffs are well aware of it from the documents upon which they rely, plaintiffs do not even mention in their Complaint GSK's Balanced Cohort Study, which showed that Avandia presented ***no increased risk*** of cardiac ischemia. Therefore, based on the ***totality*** of available data at the time, the FDA, like GSK, had not been able to determine the clinical significance of GSK's meta-analysis.[49]

Given that GSK submitted the meta-analysis to the FDA, and the Agency chose to fully evaluate its clinical significance before taking any action because "the data . . . were inconsistent," there is no adequately alleged basis to find that the meta-analysis results, alone, were "sufficiently serious and frequent to affect future earnings." *Carter-Wallace I*, 150 F.3d at 157; *see also Carter-Wallace II*, 220 F.3d at 42 (concluding that defendants was under no duty to

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[48] Paragraph 27 of the Complaint alters this quotation by taking out the phrase "because the data from the pooled analysis and the population based study were inconsistent," making it seem as though the FDA delayed for no reason other than its desire to look at the data itself.

[49] Contrary to the plaintiff's distorted description of the FDA's "safety alert" on May 21, 2007, (Compl. ¶ 31), the FDA did ***not*** state on May 21, 2007 that Avandia was, in fact, associated with any increased risk of heart attack, and instead made clear that the data were inconsistent:

> The [FDA] is aware of a potential safety issue related to Avandia (rosiglitazone), a drug approved to treat type 2 diabetes. Safety data from controlled clinical trials have shown that there is a potentially significant increase in the risk of heart attack and heart-related deaths in patients taking Avandia. ***However, other published and unpublished data from long-term clinical trials of Avandia, including an interim analysis of data from the RECORD trial (a large, ongoing, randomized open label trial) and unpublished reanalyses of data from DREAM (a previously conducted placebo-controlled, randomized trial) provide contradictory evidence about the risks in patients treated with Avandia.***
>
> * * *
>
> FDA's analyses of all available data are ongoing. FDA has not confirmed the clinical significance of the reported increased risk in the context of other studies. . . .

(Exh. 26, FDA Safety Alert.)

disclose adverse event reports prior to FDA and company jointly agreeing that the medication should be withdrawn from the market). Absent some indication from the FDA that it believed the data presented a significant safety concern, it would be unreasonable to "expect [a pharmaceutical manufacturer] to abandon its product," *Carter-Wallace II*, 220 F.3d at 42, and, therefore, otherwise factually accurate statements about a product's performance, and opinions about its future prospects, cannot possibly be fraudulently misleading. Put simply, the Complaint fails to allege any duty to disclose the meta-analyses.

B. The Complaint Fails To Plead The Requisite Strong Inference Of Scienter

The PSLRA requires that a Rule 10b-5 complaint "state with particularity facts giving rise to a ***strong*** inference" of scienter. 15 U.S.C. § 78u-4(b)(2) (2007) (emphasis added). Recently, in *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, the United States Supreme Court "mandated a uniform construction of the strong inference standard in light of the objectives of the PSLRA." *Winer Family Trust v. Queen*, 503 F.3d 319, 326 (3d Cir. 2007). Specifically, the Court held that, to qualify as "strong" under the PSLRA, "an inference of scienter must be more than merely plausible or reasonable – it must be cogent and at least as compelling as any opposing inference of nonfraudulent intent." *Tellabs*, 127 S. Ct. at 2504-05. As the Court explained, "Congress did not merely require plaintiffs to . . . allege facts from which an inference of scienter rationally *could* be drawn. Instead, Congress required plaintiffs to plead with particularity facts that give rise to a 'strong'—*i.e.*, a ***powerful*** or ***cogent***—inference." *Id.* at 2510 (second and third emphases added). The Court stressed that this inquiry "is inherently comparative." *Id.* "To determine whether the plaintiff has alleged facts that give rise to the requisite "strong inference" of scienter, a court must consider plausible nonculpable explanations for the defendant's conduct, as well as inferences favoring the plaintiff." *Id.*

Accordingly, under *Tellabs*, courts must follow three steps to determine whether a plaintiff has surmounted the "significant bar to litigation" imposed by the PSLRA's scienter pleading requirement. *Globis Capital Partners, L.P. v. Stonepath Group, Inc.*, No. 06-2560, 2007 WL 1977236, at *3 n.1 (3d Cir. July 10, 2007). First, the court must "accept all factual allegations in the complaint as true." *Tellabs*, 127 S. Ct. at 2509. This applies to non-conclusory allegations based on personal knowledge.[50] Second, the court "must consider the complaint in its entirety," ***including*** those additional "sources courts ordinarily examine when ruling on Rule 12(b)(6) motions to dismiss, in particular, documents incorporated into the complaint by reference, and matters of which a court may take judicial notice." *Id.* Third, "the court must take into account plausible opposing inferences" when determining "whether the pleaded facts give rise to a 'strong' inference of scienter." *Id.*

A plaintiff may satisfy the scienter requirement by alleging specific "facts (1) showing that the defendants had both a motive and opportunity to commit the fraud or (2) constituting strong circumstantial evidence of conscious misbehavior or recklessness." *ATSI Commc'ns, Inc. v. Shaar Fund, Ltd.*, 493 F.3d 87, 99 (2d Cir. 2007).[51] In cases like this, where the plaintiff has alleged a misleading omission, the relevant recklessness inquiry is "not merely whether [the defendant] had knowledge of the undisclosed facts; rather, it is the '*danger of misleading buyers* [that] must be actually known or so obvious that any reasonable man would be legally bound as knowing.'" *City of Phila. v. Fleming Cos.*, 264 F.3d 1245, 1261 (10th Cir.

[50] The Complaint states that the only allegations that are based on personal knowledge are those relating to the plaintiffs themselves and that "as to all other matters," it is based on information and belief. (Compl. at p. 1.) To be credited, those information and belief allegations must be supported by all facts on which they are formed. *See* 15 U.S.C. § 78u-4(b)(1).

[51] The *Tellabs* Court specifically reserved the question of whether pleading recklessness is sufficient to satisfy the "intent to deceive, manipulate or defraud" standard. 127 S. Ct. 2499, 2507 n.3 (2007).

2001) (citing *Schlifke v. Seafirst Corp*., 866 F.2d 935, 946 (7th Cir. 1989)) (emphasis added); *accord CP St. Louis Casino LLC v. Casino Queen Inc.*, No. 07-CV-447, 2007 WL 3119828, at *5 (S.D. Ill. Oct. 23, 2007); *In re Discovery Labs. Sec. Litig.*, No. 06-1820, 2006 WL 3227767, at *14 (E.D. Pa. Nov. 1, 2006); *Wilson v. Bernstock*, 195 F. Supp. 2d 619, 638-39 (D.N.J. 2002). In other words, knowledge can be shown only by demonstrating that the fact "was so obviously material that the defendant must have been aware both of its materiality and that its non-disclosure would likely mislead investors." *Fleming*, 264 F.3d at 1261.

Here, plaintiffs fail to plead scienter adequately under either test, and the Complaint should be dismissed. 15 U.S.C. § 78u-4(b)(3)(A).

1. Plaintiffs Have Not Alleged That Defendants Had Any Conscious Intent to Defraud By Concealing Information

As discussed in Section 2, below, plaintiffs have not alleged any "motive and opportunity" for defendants to have engaged in a fraud. Thus, a stricter standard applies to their attempts to "'plead scienter by identifying circumstances indicating conscious behavior [or recklessness] by defendant. . . . " *In re eSpeed, Inc. Sec. Litig.*, 457 F. Supp. 2d 266, 281-82 (S.D.N.Y. 2006) (citing *Kalnit v. Eichler*, 264 F.3d 131, 143 (2d Cir. 2001)). Here, plaintiffs have not pleaded any such circumstances.

Specifically, to avoid dismissal as to statements of historical fact, a complaint must allege conduct "which is 'at the least . . . highly unreasonable and which represents an extreme departure from the standards of ordinary care to the extent that the danger was either known to the defendant or so obvious that the defendant must have been aware of it.'" *Kalnit*, 264 F.3d at 142 (*quoting Carter-Wallace II*, 220 F.3d at 39). "The pleading requirements for conscious misbehavior or recklessness generally impose on plaintiffs the burden of alleging that defendants had knowledge of specific facts or documents that they disregarded. Such lack of

specificity ordinarily is fatal to a plaintiff's effort to plead scienter based on conscious misbehavior or recklessness." *In re Rhodia S.A. Sec. Litig.*, No. 1:05-CV-5389, 2007 WL 2826651, at *21 (S.D.N.Y. Sept. 27, 2007) (internal quotations and citations omitted). As discussed in Section III.C, below, the standard is even higher with respect to forward looking statements, as plaintiffs must allege that the defendants actually knew that they had a duty to disclose the allegedly omitted information.

Here, the Complaint comes nowhere close to satisfying the stringent pleading standard of recklessness, much less actual knowledge. Indeed, application of the principles enunciated in *Tellabs* results in only one conclusion: The defendants' conduct here was completely innocent.

Simply put, plaintiffs' theory makes no sense. First, GSK disclosed its meta-analysis results to the FDA (and to other regulatory bodies, such as the EMEA) ***and*** posted the data on its CTR, conduct which hardly suggests an intent to defraud by concealing information. (*See supra* Section II.B.5.) Dr. Nissen himself used materials from GSK's CTR in his meta-analysis, and reviewed GSK's own meta-analysis while "scrolling through" the CTR. (*See supra* Section I.)

Second, the FDA itself questioned the significance of GSK's meta-analysis in light of "***other published and unpublished data from long-term clinical trials of rosiglitazone provid[ing] contradictory evidence***." (Exh. 26, FDA Safety Alert (emphasis added).) Although plaintiffs consistently conflate knowledge of the results of the GSK meta-analysis with knowledge of "risk" to Avandia users, (*e.g.*, Compl. ¶¶ 25-28), the Complaint does not contain a single factual allegation suggesting that any of the Individual Defendants or anyone else at GSK considered Avandia dangerous based on the meta-analysis results or any other data. There is

good reason for that omission. Even today, the risk, if any, associated with Avandia is unclear. Although the FDA elected in November 2007 to require an expanded "boxed" warning on Avandia's label, it simultaneously advised that "[it was] keeping Avandia on the market because [it had] concluded that ***there isn't enough evidence that the risk is higher for Avandia than for other types of treatment.***" (Exh. 28, FDA Boxed Warning Press Release.) The warning itself will advise doctors and patients that "***the available data on the risk of myocardial ischemia are inconclusive."*** (*Id.*) In other words, no one – including the federal agency with regulatory authority over the U.S. pharmaceutical industry – is certain what, if anything, the various studies have revealed about Avandia's safety profile with respect to heart attacks.

As discussed in Section IV.A.2., above, in the absence of some reason to believe that future viability of a product is in jeopardy, a pharmaceutical company has no obligation to disclose safety information about a medication. *See In re Bayer AG Sec. Litig.*, No. 03-CV-1546, 2004 WL 2190357, at *10 (S.D.N.Y. Sept. 30, 2004); *see also, e.g., Oran v. Stafford*, 226 F.3d 275, 284 (3d Cir. 2000) (finding no duty to disclose where link between medication and reported side effect was not "definitively established"). Under these circumstances, a failure to disclose to the public preliminary safety information hardly can be deemed evidence of fraudulent intent. *See Carter-Wallace II*, 220 F.3d 36 (2d Cir. 2000); *see also, e.g., Coates v. Heartland Wireless Commc'ns, Inc.*, 55 F. Supp. 2d 628, 638 (N.D. Tex. 1999) ("It cannot be strongly inferred that a person who conceals *immaterial* information acts with intent to defraud.").

Carter-Wallace II, for example, involved Felbatol, which was found to be associated with a life-threatening side effect (aplastic anemia). The Second Circuit found that, prior to the time the company – in conjunction with the FDA – concluded that doctors and

patients should be warned about the risks associated with Felbatol, plaintiffs could not establish an inference of recklessness:

> The complaint here cannot support an inference that Carter-Wallace turned a blind eye to the reports of adverse side effects. There is no indication that Carter-Wallace knew, or should have known, of the connection between Felbatol and aplastic anemia before August 1, 1994. Although this connection was subsequently made, the allegations do not support the inference that Carter-Wallace was reckless in failing to have made it earlier.

220 F. 3d. at 42.

Finally, plaintiffs' attempts to overcome the inescapable conclusion that defendants had no intent to defraud do not pass muster. Rote allegations like "[d]efendants acted with scienter in that [d]efendants knew that the public documents and statements issued or disseminated in the name of the Company were materially false and misleading," (Compl. ¶ 68), are deficient as a matter of law – most obviously for their failure to distinguish among the "defendants." Indeed, plaintiffs consistently attack the Company and the "defendants" only in the most general terms. (*See, e.g.*, Compl. ¶ 25-29.) Although plaintiffs do succeed in attributing specific statements to specific individuals (hardly a difficult task), nowhere in the Complaint do they link those same individuals to personal, contemporaneous knowledge of facts or documents arguably rendering those statements false or misleading.

> ***Scienter of the individual defendants . . . is not so easily alleged.*** . . . [G]eneral allegations regarding the magnitude of the fraud or the organizational role of a defendant are insufficient to raise a strong inference of a defendant's scienter.

In re Marsh & McClennan Cos., Inc. Sec. Litig., 501 F. Supp. 2d 452, 483 (S.D.N.Y. 2006) (internal quotation and citations omitted, emphasis added); *see also, e.g., In re Bayer AG Sec. Litig.*, 2004 WL 2190357, at *16 (holding that plaintiffs failed to "plead sufficient allegations of scienter" as to two defendants in the absence of allegations that "either of them knew of the

conclusion by other Bayer executives that the Baycol brand was at risk"); 15 U.S.C. § 78u-4(b)(2) (plaintiffs must "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind"). For this reason as well, the Complaint fails to satisfy the PSLRA scienter pleading requirement.

2. Plaintiffs' "Motive" Allegations Are Plainly Deficient

Plaintiffs characterize the allegations of paragraphs 68 through 70 of the Complaint as their "***additional*** scienter allegations." (Compl. ¶ 18 (emphasis added).) Yet, plaintiffs have not pleaded ***any*** factual allegations supporting ***any*** inference of scienter – let alone a powerful or cogent inference – ***anywhere*** in the Complaint. Although the so-called "insider trading" averments, set forth in paragraph 70, give the appearance of substance, they, too, fail to plead any inference of scienter.

Most of the stock transactions listed in paragraph 70 have nothing to do with any of the Individual Defendants and, for this reason alone, cannot satisfy plaintiffs' burden to "state with particularity facts giving rise to a strong inference that [any] ***defendant*** acted with the required state of mind." 15 U.S.C. § 78u-4(b)(2) (emphasis added). Conversely, plaintiffs have not identified ***any*** sale transactions by two of the four Individual Defendants – Messrs. Bicknell and Heslop, and, therefore, have made ***no*** motive allegations as to these defendants. Furthermore, neither the Complaint nor the associated SEC filings reveal anything unusual or suspicious about the relatively few stock sales the other two Individual Defendants – Dr. Garnier and Mr. Stout – made. To the contrary, the SEC filings show that both defendant Garnier and defendant Stout, as well as defendant Heslop, ***increased*** their holdings during the putative Class Period. Thus, plaintiffs' "insider trading" allegations fail to show a motive to commit fraud.

(a) Plaintiffs Misrepresent The Scope Of The Stock Sale Transactions Associated With The Individual Defendants

According to plaintiffs, "the Individual Defendants sold more than 250,000 shares of their personally-held [GSK] ADSs for proceeds of approximately $27.5 million." (Compl. ¶ 70.) As a threshold matter, this statement is simply untrue.

First, plaintiffs have identified no sales by either defendant Bicknell or defendant Heslop. (*See* Compl. ¶¶ 6-13, 70.) This fact alone should defeat any "strong inference" of scienter – not only as to defendants Bicknell and Heslop but also as to all defendants. *See, e.g., In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1423 (3d Cir. 1997) (finding plaintiffs' pleading "inadequate to produce a 'strong' inference of 'fraudulent intent'" where, among other things, "two officer-defendants [were] not alleged to have traded at all"); *Acito v. IMCERA Group, Inc.*, 47 F.3d 47, 54 (2d Cir. 1995) ("The fact that the other defendants did not sell their shares during the relevant class period undermines plaintiffs' claim that defendants delayed notifying the public 'so that they could sell their stock at a huge profit.'") (*citing In re Cypress Semiconductor Sec. Litig.*, 1992 WL 394927 (N.D. Cal. 1992); *In re eSpeed, Inc. Sec. Litig.*, 457 F. Supp. 2d 266, 289 (S.D.N.Y. 2006) ("[T]he fact that neither [defendant] Chertoff nor [defendant] Lutnick sold stock during the putative class period undermines plaintiffs' motive allegations against defendants."). To plead motive, a complaint must make motive allegations that "entail concrete benefits that could be realized by one or more of the false statements and wrongful nondisclosures alleged." *Kalnit v. Eichler*, 264 F.3d 131, 139 (2d Cir. 2001) (internal quotations omitted); *accord In re Refco, Inc. Sec. Litig.*, 503 F. Supp. 2d 611, 645 (S.D.N.Y. 2007). Plaintiffs have alleged no such "concrete benefits" with respect to defendant Bicknell or defendant Heslop.

Second, of the 14 stock sale transactions plaintiffs have identified, ten were made by non-defendants, Dr. Yamada and Messrs. Greig, Louv, Phelan, and Ziegler.[52] (*See* Compl. ¶¶ 6-13, 70.) These alleged transactions account for the majority of the stock sales plaintiffs attack – approximately $21 million (76%) of the $27.5 million figure plaintiffs cite. (*See id.* at ¶ 70.) Yet, plaintiffs have neither named Dr. Yamada and Messrs. Greig, Louv, Phelan, and Ziegler as defendants nor mentioned them anywhere else in the Complaint. Having made no allegations even remotely connecting these individuals to the alleged wrongdoing, plaintiffs cannot rely on their alleged stock sales to establish the Individual Defendants' scienter. *See, e.g.*, *In re Lexar Media, Inc. Sec. Litig.*, No. C-04-2013, 2005 WL 1566534, at *6 n.1 (N.D. Cal. July 5, 2005) ("[S]tock sales by non-defendants cannot be a basis for establishing scienter unless the non-defendant intended to assist defendants.").[53]

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[52] To date, defendants have not been able to locate any public documents confirming a sale of securities by Ziegler in December 2005. Assuming this allegation is correct (as is proper on a motion to dismiss), it is nevertheless irrelevant. *See infra* Section IV.B.2(b).

[53] *See also In re Marsh & McLennan Cos., Inc. Sec. Litig.*, 501 F. Supp. 2d 452, 485 (S.D.N.Y. 2006) ("Plaintiffs adequately allege that certain non-defendant employees engaged in misconduct and that the existence of improper conduct within the Company made certain public disclosures false. But Plaintiffs can not use this information to allege the Senior Management Defendants' scienter without adequate factual allegations that *those* defendants *engaged* in misconduct or *knew* that their disclosures were false."); *In re Century Business Servs. Sec. Litig.*, No. 1:99-CV-02200, 2002 WL 32254513, at *7 n.18 (N.D. Ohio June 27, 2002) ("As additional evidence of scienter, plaintiffs allege that vice-presidents Stout and Feighan sold 120,000 and 60,000 shares, respectively, on February 6, 1998 . . . and that vice-president Burdick sold 27,000 shares on August 13, 1998. Since these individuals are non-defendants under the Consolidated Complaint, however, the Court does not consider these sales probative of the defendants' scienter."); *In re Versant Object Tech. Corp. Sec. Litig.*, No. C 98-00299, 2001 WL 34065027, at *5 (N.D. Cal. Dec. 4, 2001) ("Plaintiffs include the sales of non-Defendant Pulkownik, which are irrelevant to alleging scienter against the named Defendants."); *In re Splash Tech. Holdings Inc. Sec. Litig.*, 160 F. Supp. 2d 1059, 1082 n.22 (N.D. Cal. 2001) ("The [Second Amended Complaint] does not allege specific facts, however, indicating that either [non-defendant] personally possessed non-public adverse information. Accordingly, the Court finds no reason to consider their sales in determining the scienter of the named defendants."); *In re PetSmart, Inc. Sec. Litig.*, 61 F. Supp. 2d 982, 1001 (D. Ariz. 1999) ("[W]e reject plaintiffs' efforts to bolster the perception of 'insider trading' by pleading the stock sales of unnamed defendants during the class period. Without specific facts suggesting that defendants intended their manipulation of PetSmart's stock to assist these specific colleagues, we find no reason to consider these transaction."); *Plevy v. Haggerty*, 38 F. Supp. 2d 816, 834 n. 12 (C.D. Cal. 1998) ("It is unclear to the Court why Plaintiffs included sales by unnamed insiders. Their transactions are irrelevant to alleging scienter against the five named Defendants."); *In re Silicon Graphics, Inc. Sec. Litig.*, 970 F. Supp. 746, (N.D. Cal. 1997) ("In evaluating defendants' scienter, the [PSLRA] requires the Court to consider each defendant's sales separately.") (citing 15 U.S.C. § 78u-4(b)(2)).

In short, the only arguably relevant stock sales are four sales by defendants Garnier and Stout for "proceeds" (***not*** profits) of less than $6.5 million.[54] As explained below, however, these sales do not give rise to any inference of scienter, much less a strong one.

(b) Plaintiffs' Allegations Of Minimal Stock Sales By Individual Defendants Garnier And Stout During The Proposed Class Period Do Not Give Rise To An Inference Of Scienter

(i) Plaintiffs' Failure To Plead Any Facts Regarding Defendants' "Prior Trading Practices," Alone, Precludes A Finding That The Trading Alleged Here Is "Unusual" Or "Suspicious"

It is well-settled that "executive stock sales, standing alone, are insufficient to support a strong inference of fraudulent intent." *Malin v. XL Capital Ltd.*, 499 F. Supp. 2d 117, 150 (D. Conn. 2007) (internal quotation and citation omitted). Rather, "insider trading is suspicious only when it is dramatically out of line with prior trading practices at times calculated to maximize the personal benefit from undisclosed inside information." *Id.* (internal quotation and citation omitted). Thus, the scienter inquiry – where it rests on allegations of insider trading – necessarily requires a point of comparison: Are the defendant's stock transactions during the putative Class Period unusual or suspicious ***relative to*** the same defendant's stock transactions outside the Class Period?

The bare allegation in paragraph 70 that the Individual Defendants' sales were "unusual and suspicious" does not make it so, and the Complaint is devoid of any factual assertions that would support such a conclusion. *See, e.g., In re K-tel Int'l, Inc. Sec. Litig.*, 300 F.3d 881, 896 (8th Cir. 2002) ("[C]onclusory statements that the insider sales were unusual or

[54] As the *eSpeed* court noted, "proceeds" and "profits" are two different things. 457 F. Supp. 2d at 290 ("[P]laintiffs plead that Amaitis and Noviello realized 'gross proceeds' of $2.8 million, but the Complaint does not disclose whether either made any *profit* from the sales.").

suspicious . . . . are insufficient."). To the contrary, plaintiffs have "allege[d] only the number of shares each executive sold, the share price on the date sold, and the gross [proceeds] realized from each sale." *Malin*, 499 F. Supp. 2d at 151. This "minimalist" approach to pleading is legally deficient. It is "impossible . . . to determine [from the Complaint] whether the sales [alleged]" were unusual or suspicious in any way. *Id.; see also, e.g., K-tel*, 300 F.3d at 896 ("The Class failed to allege the prior history of sales for the defendants or even the number of shares held by each. Therefore, the Class failed to allege facts to show the trading activity was unusual or how it was unusual.") (citations omitted); *Ronconi v. Larkin*, 253 F.3d 423, 435-36 (9th Cir. 2001) (finding that, even where defendant sold 98 percent of her company stock, plaintiffs "[had] not alleged sufficient trading history for [the court] to conclude that her trading was 'dramatically out of line with prior trading practices'"); *Greebel v. FTP Software, Inc.*, 194 F.3d 185, 207 (1st Cir. 1999) (holding that where, among other things, "[p]laintiffs provided no information on sales by corporate insiders at times outside the Class Period . . . . the district court correctly concluded that plaintiffs produced no evidence that the trading was out of the ordinary or suspicious").[55] Therefore, plaintiffs have failed to satisfy their burden of proof on this essential element of their claim.

(ii) Plaintiffs Also Cannot Rely On Dr. Garnier's And Mr. Stout's Sales "In Isolation" As Evidence Of Motive

As set forth above, plaintiffs' reliance on a few isolated stock sales fatally undermines their case. Pleading a more complete picture of the Individual Defendants' stock

[55] Plaintiffs also make no effort in the Complaint to connect any defendant's transactions with any particular event (such as an alleged misstatement or omission or a peak in stock price) that conceivably could render them otherwise "suspicious." Their motive allegations fail for this reason as well. *E.g., Ressler v. Liz Claiborne, Inc.*, 75 F. Supp. 2d 43, 60 (E.D.N.Y. 1998) (noting that sales have to be "close[] in time to the alleged misstatements to give rise to a suspicion of fraud"), *aff'd sub nom., Fishbaum v. Liz Claiborne, Inc.*, 189 F.3d 460 (2d Cir. 1999).

trades, however, would have been equally damaging to plaintiffs. The simple fact is that the three Individual Defendants who traded in GSK ADSs ***increased***, not decreased, their holdings during the proposed class period.[56]

Dr. Garnier, for example, did sell 45,500 ADSs on October 30, 2006, as plaintiffs allege. Plaintiffs fail to mention, however, that the same Form 6-K documenting that sale ***also*** shows that on the very same day, Dr. Garnier exercised options on 68,411 ADSs, which options were due to expire November 20, 2006. (Exh. 4, GSK 2006 Form 6-K (filed 10/31/06).) Accordingly, Dr. Garnier was a net ***purchaser*** of approximately 23,000 ADSs. As of October 31, 2006, following both of those transactions, Dr. Garnier held 529,769.32 ADSs. (*See id.*) Similarly, the Complaint correctly alleges that Dr. Garnier sold 51,100 ADSs on February 8, 2007. Again, however, plaintiffs omit the fact that he simultaneously exercised options on 68,411 ADSs, which options were due to expire on March 24, 2007, and that following those two transactions, he held 556,198 ADSs – valued at 17 times his annual salary. (*See* Exh. 8, GSK Form 6-K (filed 02/09/07).)

Following the further sale of 17,411 ADSs on February 13, 2007, Dr. Garnier's holdings remained "equivalent to more than 17 times his annual basic salary." (Exh. 6, GSK Form 6-K (filed 02/13/07).). Even if one treats his February 13, 2007 sale as wholly unconnected with Dr. Garnier's exercise of options just a few days earlier, that sale represented barely three percent of his holdings at the time – a figure that courts routinely find will not support an inference of scienter. *See, e.g.*, *Acito v. IMCERA Group, Inc.*, 47 F.3d 47, 54 (2d Cir.

[56] Attached as Exhibit 46 are charts showing the changes in GSK holdings for Individual Defendants Garnier, Heslop and Stout during the putative Class Period. The back-up for each chart, consisting of Forms 6-K filed with the SEC, are attached as Exhibit 46 (A) (for Dr. Garnier), Exhibit 46 B (for Mr. Heslop and his spouse), and Exhibit 46 C (for Mr. Stout).

1995) (finding that complaint failed to support a "strong inference" of scienter where, among other things, defendant's sale of 30,000 shares represented less than 11% of his holdings); *Rothman v. Gregor*, 220 F.3d 81, 94 (2d Cir. 2000) (finding sales amounting to $1.6 million and $20 million returns were not unusual where the percentage of shares sold – 9.9% and 9.3% respectively – was small); *In re Initial Public Offering Sec. Litig.*, 241 F. Supp. 2d 281, 368 (S.D.N.Y. 2003) (dismissing "Rule 10b-5 claims against those sixteen Defendants who sold less than ten percent of their holdings" because such trades were "insufficiently 'unusual' to permit an inference of scienter").[57]

As to Individual Defendant Stout, the lone sale transaction plaintiffs identify was similarly associated with a net ***increase*** in his stock holdings: On February 8, 2007, although Stout sold 3,475 ADSs, he also exercised options to purchase 4,951 ADS (which options were due to expire on March 24, 2007). (Exh. 8, GSK Form 6-K (filed 02/09/07).) And he, too, held more ADSs at the end of the proposed class period than at the beginning.[58] (*See* Exh. 46 (C).)

As courts have recognized repeatedly, there is nothing suspicious about these defendants' behavior. *E.g.*, *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1424 (3d Cir. 1997) ("A large number of today's corporate executives are compensated in terms of stock and stock options. It follows then that these individuals will trade those securities in the normal course of events. We will not infer fraudulent intent from the mere fact that some officers sold

[57] As one district court has noted, there is some disagreement as to what holdings appropriately may be considered in calculating the scope of a defendant's sale. *eSpeed*, 457 F. Supp. 2d at 291. Here, however, whether one includes or excludes "earned but deferred shares," Dr. Garnier's February 13, 2007 sale is *de minimis*. As set forth in the text above, including earned but deferred shares, the sale represented approximately three percent of his total holdings. (Exh. 8, GSK Form 6-K (filed 02/09/07).) Excluding earned but deferred shares, the sale was less than six percent of his holdings—still well below levels that courts have considered significant in analyzing scienter.

[58] Defendant Heslop (as to whom plaintiffs have identified no sales) likewise increased his ordinary share holdings over the course of the proposed class period. (*See* Exh. 46 (B).)

stock.") (citation omitted); *Commc'n Workers of Am. Plan for Employees Pensions & Death Benefits v. CSK Auto Corp.*, No. CV06-1503-PHX-DGC, 2007 WL 951968, at *7 (D. Ariz. Mar. 28, 2007) ("Defendants also note that all but 2% of the stock sold by the Individual Defendants during the Class Period involved options set to expire in a matter of months. Such sales are logical, not inherently suspicious."); *In re NTL, Inc. Sec. Litig.*, 347 F. Supp. 2d 15, 31 (S.D.N.Y. 2005) ("Blumenthal's sale of 93,148 shares in April 2000 only weeks before exercising an option to buy 7.25 million shares in the following month is not suggestive of a desire to get rid of his holdings in advance of the disclosure of bad news. Accordingly, the allegation of Blumenthal's sale does not justify an inference of scienter."); *In re Bristol-Meyers Squibb Sec. Litig.*, 312 F. Supp. 2d 549, 561 (S.D.N.Y. 2004) ("[T]he documents reflecting the Individual Defendants' trading in BMS stock during the Class Period show a consistent pattern of trading undertaken primarily to make payments required for the exercise of stock options or to pay taxes. In fact . . . the Individual Defendants, in almost every instance, *increased* their BMS holdings during the Class Period—a fact wholly inconsistent with fraudulent intent.") (citations and footnote omitted); *Campbell v. Lexmark Int'l Inc.*, 234 F. Supp. 2d 680, 687 (E.D. Ky. 2002) ("[F]ar from 'suspicious,' Mann's stock sales seem perfectly reasonable in light of the impending expiration of many of his stock options.").

Simply put, plaintiffs' portrayal of the Individual Defendants' stock sale transactions as evidence of fraud utterly ignores the documented circumstances in which those transactions took place. As such, the Complaint fails to offer even a "plausible" inference of fraudulent intent. *Tellabs*, 127 S. Ct. at 2510. It certainly does not offer a "powerful or cogent" inference. *Id.* The Complaint should be dismissed.

C. To The Extent They Are Based on Forward-Looking Statements, Plaintiffs' Claims Are Not Actionable Under The PSLRA's Safe Harbor Provision

Many of the statements that plaintiffs challenge are forward-looking statements regarding Avandia's expectations and growth potential. (*See, e.g.*, Compl. ¶¶ 44, 46, 47, 49, 51, 56, and 62.) The PSLRA creates a "safe harbor" for forward-looking statements like these, which requires plaintiffs to allege and prove, *inter alia*, that such statements were made with "actual knowledge" that the statements were false or misleading. *See* 15 U.S.C. § 78u-5(c)(1)(B) (2007). As shown above, plaintiffs have not come close to pleading that any defendant acted with recklessness, much less "***actual knowledge***." Accordingly, the Complaint must be dismissed under the PSLRA safe harbor provision.

Under the PSLRA's safe harbor, a reporting company and its officers, directors and employees may not, as a matter of law, be held liable for predictions or other forward-looking statements which later prove to be inaccurate if:

(1) the forward-looking statement is "identified as a forward-looking statement, and is accompanied by meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the forward-looking statement" (15 U.S.C. § 78u-5(c)(1)(A)(i)); or the forward-looking statement is "immaterial" (15 U.S.C. § 78u-5(c)(1)(A)(ii)).

or

(2) the plaintiff fails to prove the forward-looking statement was made, or approved by an executive officer of the company, with actual knowledge that the statement was false or misleading. (15 U.S.C. § 78u-5(c)(1)(B)).

Thus, the safe harbor affords defendants two alternative bases upon which to protect themselves from liability for forward-looking statements. Because these two prongs operate independently of each other, if one prong of the safe harbor is met, plaintiffs' claims must be dismissed. *See Fellman v. Electro Optical Sys. Corp.*, No. 98-civ-6403 LBS, 2000 WL

489713, at *4-6 (S.D.N.Y. Apr. 25, 2000) (granting motion to dismiss on basis that specific statements were protected by the "actual knowledge" prong of the PSLRA's safe harbor).

According to the Complaint, the forward-looking statements are set forth in documents such as: (1) October 27, 2005 Conference Call (*Id.* ¶ 44); (2) February 8, 2006 6-K (*Id.* ¶ 46); (3) February 8, 2006 Conference Call (*Id.* ¶ 47); (4) March 3, 2006 Form 20-F (*Id.* ¶ 49); (5) April 27, 2006 Form 6-K (*Id.* ¶ 51); (5) October 26, 2006 Conference Call (*Id.* ¶ 56); and (6) March 2, 2007 Form 20-F (*Id.* ¶ 62). These statements fall squarely within the PSLRA's definition of a "forward-looking statement" because they relate to "statement[s] of future economic performance" or "statements of the plans and objectives of management." 15 U.S.C. § 78u-5(i)(1). For example, plaintiffs challenge the following statements in GSK's 2005 Annual Report: (1) "Looking into 2006, the strong growth seen from key products [including Avandia] and from our vaccines business is expected to continue" (Compl. ¶ 49); and (2) "The strong growth seen from key products such as Seretide/Advair, Avandia/Avandemet and from GSK's vaccines business is expected to continue in 2006." (*Id.*) Plaintiffs also challenge the following statement in GSK's 2006 Annual Report: "Looking ahead, we expect new clinical data to help deliver growth from Seretide/Advair and the Avandia group of products, and continued good performance from our vaccines business." (*Id.* ¶ 62.) These types of statements clearly fall within the ambit of the PSLRA's definition of a "forward looking statement."

Further, these statements include words or phrases regarding the future such as: "expect," "expected," "looking into," "prepared," and "looking ahead." (*See*, *e.g.*, *id.* ¶¶ 44, 46, 47, 49, 51, 56, and 62.) Because of the use of these words of futurity, the truth or falsity of these statements can only be determined based on events to occur in the future, after each statement has been made. As such, under the PSLRA, these statements are forward-looking.

Finally, these forward looking statements generally contained specific language identifying the statements as forward looking. For example, a press release containing a challenged statement, that is included as an exhibit to the February 8, 2006 Form 6-K states:

> Under the safe harbor provisions of the US Private Securities Litigation Reform Act of 1995, the company cautions investors that any forward-looking statements or projections made by the company . . . are subject to risks and uncertainties that may cause actual results to differ materially from those projected.

(Exh. 19, GSK Press Release, Preliminary Announcement of Results for the year ended 31st December 2005 (Feb. 8, 2006) at 1.)

Moreover, as to these statements, GSK provided meaningful cautionary language in its filings with the SEC. In the documents containing the forward-looking statements, GSK specifically directed the investment community and general public to risk factors in its annual report that could cause "actual results to differ materially from expected and historical results." (Exh. 9, GSK 2006 Form 20-F (filed 03/02/07, at 44.) The annual report notes, for example, that with respect to new products, some products may "have only limited commercial success as a result of efficacy or safety concerns. . . ." (*Id*. at 44-45.) Further, regarding product liability litigation, GSK warned that "when drugs and vaccines are introduced into the marketplace, unanticipated side effects may become evident." (*Id.*) This cautionary language protected the statements under the first prong of the safe harbor.

But even if there were no cautionary language, the second prong of the PSLRA's safe harbor provision provides protection if plaintiffs fail to prove that defendants' forward-looking statements were made with ***actual knowledge*** that each such statement was false or misleading. 15 U.S.C. § 78u-5(c)(1)(B) (emphasis added). Significantly, "[a]n even more stringent scienter requirement applies to forward-looking statements . . . where plaintiffs must plead facts to support the strong inference that the speaker had actual knowledge that the

statement was false or misleading when made." *In re Eastman Kodak Co.*, No. 6:05-CV-6326, 2006 WL 3149361, at *4 (W.D.N.Y Nov. 1, 2006); *see also High View Fund, L.P. v. Hall*, 27 F. Supp. 2d 420, 427 (S.D.N.Y. 1998). Given plaintiffs' failure (detailed above) to plead any facts showing that Defendants acted with recklessness, they certainly have not alleged facts showing actual knowledge.

In fact, contrary to this actual knowledge requirement, plaintiffs generally fail to plead in even conclusory form that defendants acted with actual knowledge.[59] Instead, plaintiffs conclusorily plead that defendants were unreasonable or reckless. For example, plaintiffs plead: "Based on this adverse information, coupled with the results from the First Meta-Analysis [preliminary meta-analysis], Defendants lacked a reasonable basis for their positive statements" (Compl. ¶ 50) and "Defendants knew or recklessly disregarded the falsity and misleading nature of the information which they caused to be disseminated to the investing public." (*Id.* ¶ 69.) Recklessness or unreasonableness are not enough.

Although plaintiffs sprinkle a few general allegations of actual knowledge into the Complaint (*see, e.g.*, *id.* ¶ 68 ("Defendants knew that the public documents and statements issued or disseminated in the name of the Company were materially false or misleading.")), such general allegations do not suffice. Indeed, courts have routinely dismissed claims under the PSLRA's "actual knowledge" prong because of general allegations similar to those asserted by plaintiffs here. For example, in *Fellman v. Electro Optical Systems Corporation*, the court held that forward-looking statements were protected by the PSLRA's safe harbor because the

[59] Notably, plaintiffs even challenge forward-looking statements that turned out to accurate predictions and projections. For example, the following projection turned out to be accurate for the product: "Looking into 2006, the strong growth seen from key products [including Avandia] and from our vaccines business is expected to continue." (Compl. ¶ 49.) Accurate statements like these were clearly not made with actual knowledge of there false or misleading nature.

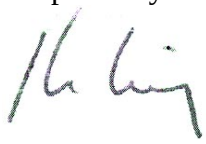
plaintiffs only alleged "in a general way that [the defendants] had actual knowledge of the falsity" but alleged "no specific facts from which such actual knowledge [could] be inferred." No. 98-CV-6403, 2000 WL 489713, at *5 (S.D.N.Y. Apr. 25, 2000); *see also In re Aegon N.V. Sec. Litig.*, No. 03-CV-0603, 2004 WL 1415973 , at *12 (S.D.N.Y. 2004) ("Here, the Plaintiffs only generally allege that the Defendants had actual knowledge of the alleged falsity of their statements . . . without alleging specific facts to support such an inference.").

Thus, the safe harbor of the PSLRA provides yet another reason why plaintiffs' Complaint should be dismissed.

V. CONCLUSION

For all of the above reasons, defendants respectfully request that the Court dismiss plaintiffs' Amended Complaint in its entirety and with prejudice.

Respectfully submitted:



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